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SECOND ATTACKS OF ACUTE POLIOMYELITIS, AND THE MINIMAL DURATION OF IMMUNITY

BY

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Acute anterior poliomyelitis, like some other diseases due to a specific infection, seems to confer immunity for a time. At present there is but little evidence to show how long this immunity lasts. There is proof, in the occurrence of second attacks, that it is not always permanent.

The late Dr. F. E. Batten[1], in his Lumleian lectures on acute poliomyelitis (1916), said that no instance of a second attack had come under his observation. Referring to three cases reported by Oulmont and Baudouin[2], Eshner[3], and Sanz[4], he said ' not one of these cases appears to me to be convincing or to bear critical investigation.' I had independently come to the same conclusion with regard to the case reported by Oulmont and Baudouin ; and Eshner himself regarded the nature of the second attack in his own case as doubtful ; the third case, by Sanz, I have included in a series of collected cases as one of reasonable probability.

After exclusion of the two doubtful cases I have been able to find only eight recorded cases in which there seemed to be a clear history of a second attack of acute poliomyelitis (see Table).

To this list may be added the following case.

Dorothy V., aged 7½ years, was admitted to King's College Hospital on October 14th, 1929. At the age of 1¾ years she had an attack of acute poliomyelitis which left her with a wasted and paralysed left leg, so that she was obliged to wear an iron support for walking and is still crippled.

At 7½ years old, on September 30th, 1929, she stumbled in walking and fell, but did not hurt herself badly. On the night of October 1st, she had pain in the back of the neck, and was feverish and sweated. The pain persisted, so that she was kept in bed for three days. On October 5th she went out in the garden and fell down, and found she could not pick herself up. Her walking was as it had been before, but she now found that if she sat on the floor she could not get herself up into the standing position. The reason was obvious when she was admitted to hospital, for the muscles of the right shoulder were found to be paralysed. She could not abduct the arm, nor raise it so as to put her hand on her head. Flabbiness and then wasting appeared, especially in the right supra-spinatus and deltoid muscles, and five weeks after admission there was reaction of degeneration in the deltoid, and the reaction in the infra-spinatus was diminished both to faradism and galvanism. Ten weeks after admission there was visible wasting of the right infra-spinatus and supra-spinatus, and especially of the deltoid muscle : there was considerable recovery of movement, the child could now put her right hand on the top of her head with some special effort. There was no affection of the rest of the limb.

So far as can be judged from clinical evidence this case appears to be a clear instance of a second attack of poliomyelitis after an interval of 5¾ years.

It adds therefore to the evidence already accumulated that an attack of acute poliomyelitis does not necessarily confer permanent immunity.

This is no proof that such an attack does not confer temporary immunity; nor indeed that it does not sometimes, or even usually, confer permanent immunity. The history of other infectious diseases, even those which experience has shewn to be most highly protective, makes it unlikely that the immunity conferred by this disease should always be permanent. Second attacks have been known even in variola and varicella which are very highly protective, and whooping-cough, though it usually gives permanent immunity, does not always do so. Indeed it may be doubted whether any form of infection necessarily establishes permanent immunity.

TABLE.

REPORTED CASES OF SECOND ATTACKS OF ACUTE POLIOMYELITIS.

Case No.	Author	Sex	Ages of attacks	Interval of attacks	Parts affected
1	Caudouin[7] ..	M	17 mo., 16 yr.	14 yr.	1. L. leg. 2. R. leg.
2	Ballet & Dutil[8] ..	F	3 yr., 12 yr., 14 yr.	9 yr. 2 yr.	1. L. leg. 2. Both arms. 3. Both legs.
3	Eckert[9]			5 yr.	1. L. leg. 2. R. leg.
4	Lucas & Osgood[10]	M	2 yr., 5 yr.	2 yr.	1. Both feet and R. leg. 2. R. arm and both legs weak.
5	Sanz[4]	F	1 yr., 15 yr.	14 yr.	1. L. leg. 2. R. leg.
6	Taylor[11]	M	3 yr., 6 yr.	3 yr.	1. R. leg. 2. L. leg.
7	Francis & Moncrieff[12]	F	3 yr., 18 yr.	15 yr.	1. R. arm. 2. Both legs.
8	Peremans[13] ..	F	$2\frac{3}{4}$ yr., $4\frac{3}{4}$ yr.	2 yr.	1. L. leg. 2. One arm.
9	Author	F	$1\frac{3}{4}$ yr., $7\frac{1}{2}$ yr.	$5\frac{3}{4}$ yr.	1. L. leg. 2. R. shoulder.

Minimal duration of immunity.—If the minimal duration of immunity from a fresh infection with the virus of poliomyelitis could be determined, it would afford some guidance, during an epidemic of the disease, in the care of those children who had already had an attack of it.

In seeking to arrive at a solution of this question of duration of immunity, it is necessary to distinguish sharply between recrudescence and re-infection. A considerable number of cases have been recorded in which recurrence of symp-

toms and extension of paralysis have occurred several days or weeks after the first onset. The interval has varied from one week up to twelve weeks. Probably no one, in view of the known duration of the infection in the monkey and in the child, would suggest that these were anything but exacerbations or extensions of the original infection.

There is experimental evidence that the infection may be harboured by a child for at least four months. In Case 4 in the accompanying Table, Lucas and Osgood produced the disease in a monkey by inoculation with the nasal secretion from the child four months after his second attack. This case offers no evidence as to longer persistence of the infection, but it is stated on the authority of the Royal Medical Institute of Sweden[5] that in the epidemic which occurred in 1911 in that country, infection was proved by inoculation experiments to persist in the mouth and intestine of persons affected for periods extending up to seven months.

This, however, does not prove that the child is liable to a fresh attack of the disease during this period, for he may be immune though still a carrier; indeed the few available observations collected here seem to show that within the period during which he may still be carrying infection the child acquires, either at once or after one or more recrudescences, an immunity which has a certain minimal duration.

The minimal duration of this immunity could be determined with some degree of accuracy if large numbers of observations of second attacks were available, but the total number at present is so small that it affords only sufficient grounds for a conclusion which may have to be revised in the light of further experience.

Apart from the many cases recorded in which symptoms of acute poliomyelitis recurred or recrudesced within three months after the first onset, there is, with one very doubtful exception*, no case on record so far as I have been able to ascertain of recurrence of symptoms after an interval of three months until an interval of two years is reached: in other words there is apparently a silent period of two years between the time when recrudescence ceases to occur and the time when liability to a fresh attack begins to appear. In four out of the nine cases collected here the interval between any two attacks was 2 to 2½ years, and in another it was 3 years: the others were all after longer intervals. In one of this series (Case 2) there were three separate attacks of definite acute poliomyelitis, and the intervals between them were 9 years and 2 years. Another (Case 8) was thought to have had an abortive attack consisting only of headache, convulsion and stiffness of the neck, twelve weeks before the first paralytic attack, but the nature of the first illness is so inconclusive that it can hardly be accepted in the absence of other evidence as an attack of acute poliomyelitis: it was followed 12 weeks later by a definite attack of acute poliomyelitis, and then, after an interval of two years, by another attack of poliomyelitis.

*A boy aged 5 years had transient loss of power in both legs for two days only, after which he was quite well until 19 months later when he had an attack of paralysis in the right leg which was left permanently weak (Sheppard[6]). The nature of the earlier attack here is obviously very uncertain.

Conclusions.

It would seem that there are two groups of recurrence of poliomyelitis, chronologically distinct: those occurring within three months after the first onset, and those occurring after an interval of two years or more.

This silent period, the interval between the two groups, suggests that either as a result of the initial infection or of recrudescence of the infection within the first few weeks, an immunity is established which has a minimal duration of about two years.

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ANÆMIA AND LIVER THERAPY IN INFANCY AND CHILDHOOD

BY

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In recent years, considerable attention has been directed to the effects of liver therapy in the anæmias of adults, but the application of this in infancy and childhood does not appear to have received the attention it deserves; and while it is the object of this paper to give a general review of the anæmias occurring in early life, hæmolytic anæmias, in which liver therapy has been successful, are discussed in greater detail.

In discussing the measures essential in a given case, it is necessary to have a clear conception of the types of anæmia met with in infancy and childhood, and of the manner in which the reaction of the patient to the pathological process may affect the blood picture.

It is well recognized that in infants trivial causes may affect the temperature to a considerable extent, whereas in the adult the variation would not be noticed. This juvenile reaction is true of almost every system, but it may not be out of place to stress its importance in relation to the hæmopoietic system,——a slight infection, for example, may cause a degree of anæmia which would be alarming if met with in an adult. Whilst, in the main, the causes of anæmia are essentially the same in infants and adults, the violence of the reaction in children may cause a grave anæmia; whereas in adults the fall in hæmoglobin may be so slight that it is a matter of only minor importance. In premature infants, this reaction is especially marked.

In this paper, the following arrangement has been adopted:—

In Part 1, hæmolytic anæmias are discussed in some detail, under the following headings:—

(a) True pernicious anæmia,
(b) Acholuric jaundice,
(c) Hæmolytic anæmias obviously of infective origin,
(d) Congenital, or occurring in the early months of life.

In Part 2, a somewhat brief account is given of non-hæmolytic anæmias:—

(a) Anæmia due to hæmorrhage,
(b) Chlorotic anæmias,
(c) Grave secondary (aplastic) anæmias,
(d) Splenic anæmia,
(e) Anæmias associated with metabolic disturbances,
(f) Anæmias of infective origin,
(g) Anæmia associated with Hodgkin's disease, leukæmia, chloroma, and glandular fever,
(h) Anæmia associated with malignant disease.

Normal variations of the blood in infancy and childhood.

For purposes of comparison with anæmic states it is useful to review the normal variations of the blood picture as found in infancy and childhood. Considerable differences have been found by various workers, some of whom, however, have based their averages on comparatively few cases. A further difficulty is encountered in deciding what is to be regarded as a normal child. In discussing her findings in infancy, Helen Mackay[1] arrived at the conclusion that the majority of babies are anæmic, on the ground that the value of the hæmoglobin can be raised by the administration of iron. Her observations were chiefly on babies in London clinics. She remarks that though 'no evidence concerning other areas of the British Isles is given, the appearance of London infants compared with those in other parts of Britain would not suggest that London is peculiar in its anæmic babies.' As the remarks in this part

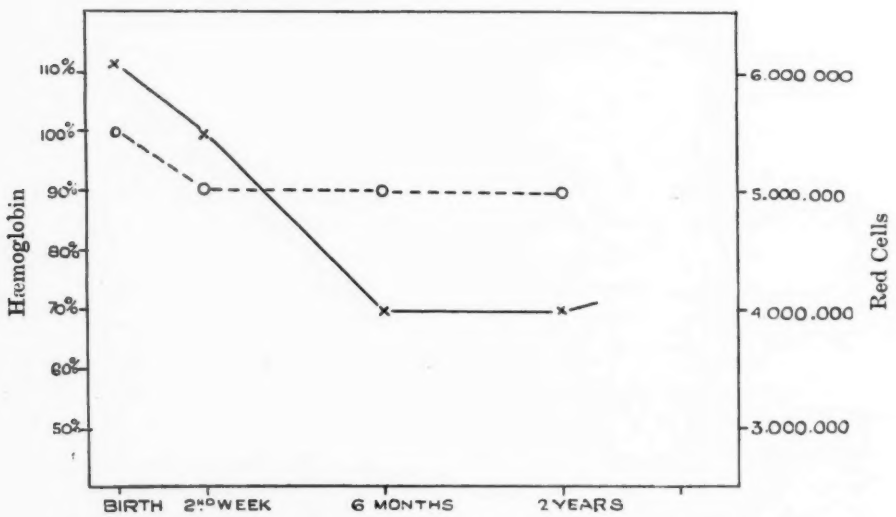

FIG. 1. Hæmoglobin (plain line) and red cell count (dotted line) in infancy (after R. Hutchison).

of the paper are introduced for comparison with states showing a considerable degree of anæmia, it appears to us that the normal should be regarded as that found in the average infant, apart from drug treatment; and these figures are given, though for purposes of further comparison the figures given by the above writer as those obtainable after the administration of iron, are also inserted.

Hæmoglobin.—All authorities are agreed that at birth the value of the hæmoglobin is high, the average being about 110 per cent. After birth this falls, reaching a value of about 70 per cent. in the third week. In some cases there may be a slight fall after this to the seventh or eighth week, after which the value remains steady until the second year (see Fig. 1). Then there appears to be a slight rise, the value at the sixth year being 75 to 80 per cent., after which it rises to the adult value. According to Helen Mackay, the values

in artificially fed babies are about 5 per cent. lower than in those breast-fed. The following figures are taken from her paper.

Fig. 2 shows the average in breast-fed and artificially fed babies not treated with iron; Fig. 3 contrasts this with the values obtained with the administration of iron.

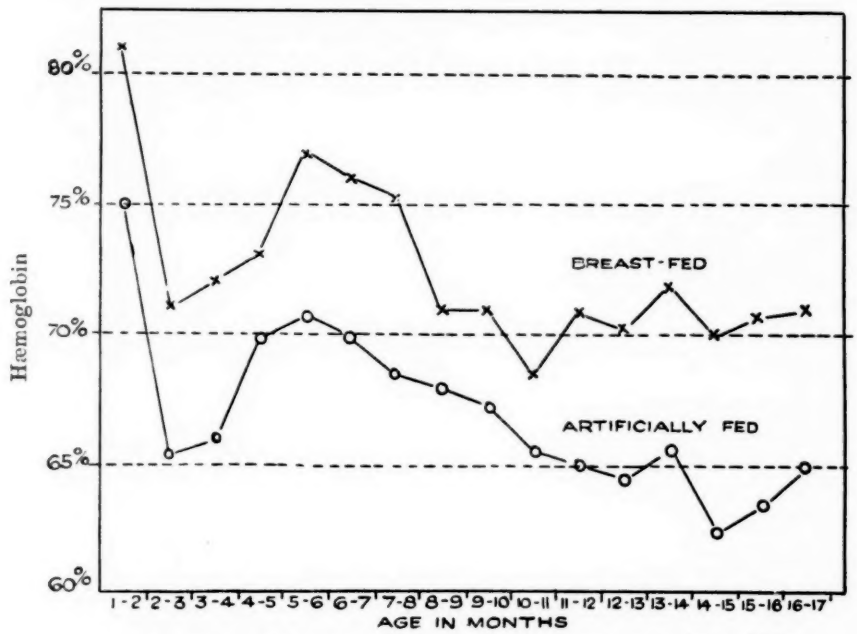

FIG. 2. Hæmoglobin values in breast-fed and artificially-fed infants.

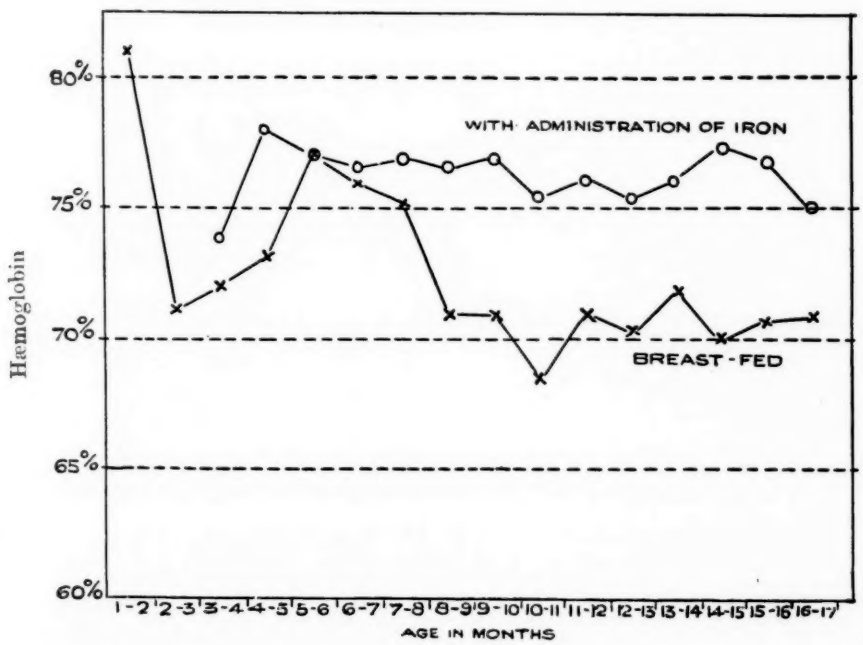

FIG. 3. Hæmoglobin values in infants with the administration of iron.

Red cells.—Fig. 4 (after Lippmann[2]) shows the changes in the red cell count during the first two days of life. According to most observers blood taken from the umbilical cord at birth gives rather higher values than those given by Lippmann for the new born. Allumbaugh[3], for example, gives 5·52 millions as the average in 50 babies : Lucas[4] gives 5·51 as the average in 36 cases and these figures are in remarkably close agreement with our own findings. From the second week onwards till the sixth year, the count appears to remain at about 5,000,000, that for both sexes being about the same (Fig. 1)[22]. During the first few days a few nucleated cells are found : some cells are irregular in shape and the variations in size are rather greater than those found in later life. Engelsen[5] states that the size of the cells in the new born is greater than in later life. We have found considerable variations, the mean diameter ranging

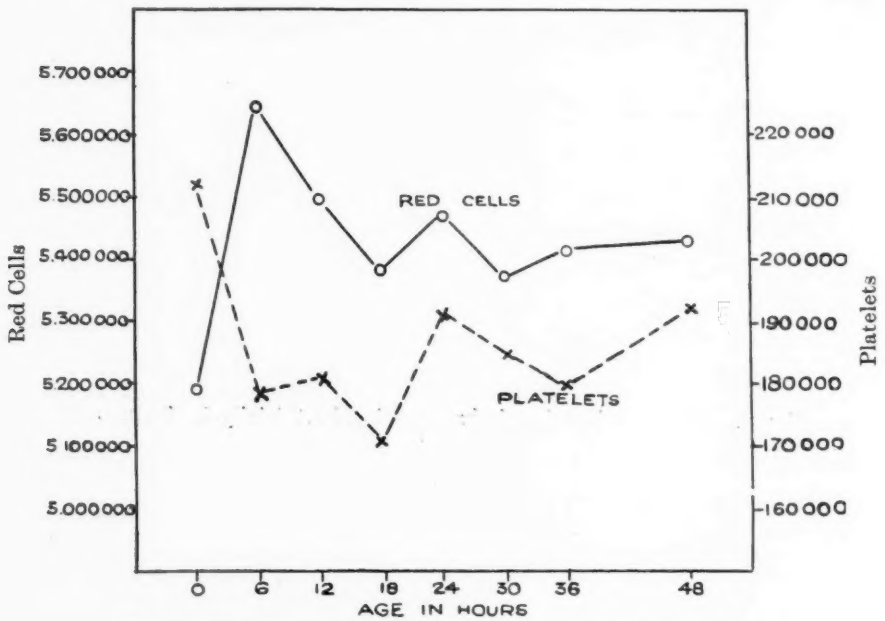

FIG. 4. Changes in red-cell and platelet count in first two days of life (after Lippmann).

from 7·3μ to 7·9μ at birth, the average being 7·6μ (normal adult value 7·23μ).

According to de Vicaris[6] the resistance of the red cells to hypotonic salines is increased at birth, but Lippmann records the opposite finding. In a large series investigated by one of us[7], the resistance of the cells was invariably found to be decreased.

White cells.—At birth the total white count averages just over 16,000, but there is a considerable variation in different individuals. Fig. 5 (after Lippmann) shows the course of the total white count, and the values of the polymorphonuclears and lymphocytes during the first five days; and Fig.6 (after Carstanjen[8]) gives similar values up to the 6th year, after which the values are those found in adults. It will be noticed that there is a fairly sharp rise in the total white count during the first twelve hours after birth : this is due entirely to an increase in the polymorphonuclear count. This rise is followed by a

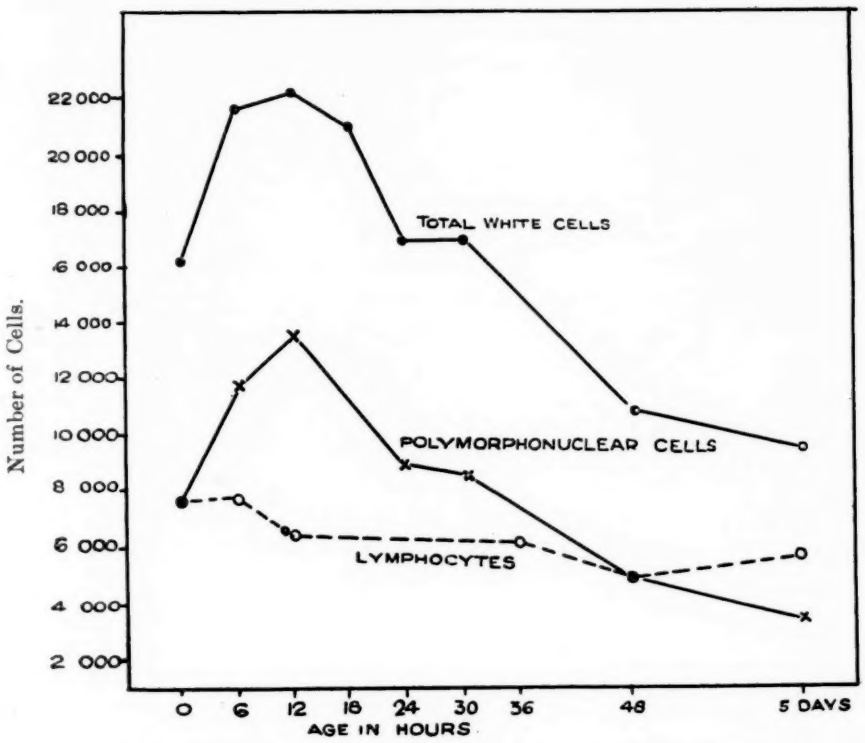

FIG. 5. Changes in white-cell count in first week of life (after Lippmann).

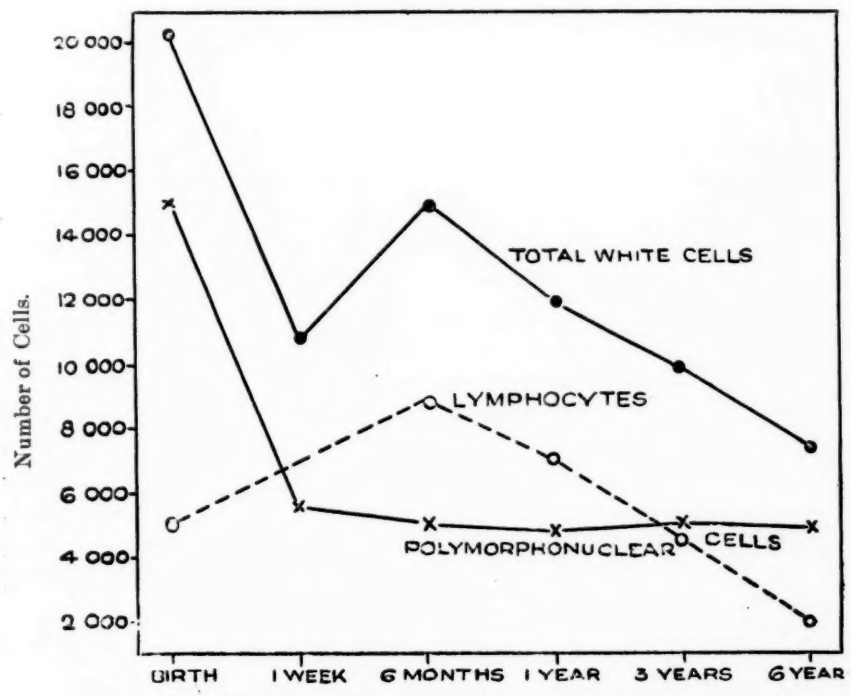

FIG. 6. Number of polymorphonuclears and lymphocytes in early childhood (after Carstanjen).

fall which continues throughout the first week of life—again due to an alteration in the polymorphonuclear count : indeed, at the end of the first week, the number of lymphocytes shows a slight rise. After the first week, the number of polymorphonuclear cells remains fairly steady at about 5,000, while the lymphocytes increase to a maximum at about the sixth month. During the first three years of life, with the exception of the first week, the number of lymphocytes is greater than that of the polymorphonuclears ; after the age of three, the number of lymphocytes continues to fall up to the age of six when adult values are obtained. This tendency to a lymphocytosis is important and it will be shown later in this paper that even in children over the age of three, stimuli which tend to produce a high white count often give rise to a relative lymphocytosis. The variations in the eosinophils and monocytes (hyalines) do not appear to be of importance. Basophils are present in small numbers during the early days of life, but by the fifth day are only occasionally observed.

Platelets.—The variations in the platelet count during the first 48 hours are shown in Fig. 4. After this time the values are approximately those found in adults.

Individual variations are least in the red cell counts, and greatest in the platelet counts. This will be seen from the coefficients of variability calculated by Lippmann from 71 infants, the variations being :—red cells 11 per cent., total white cells 25 per cent. (polymorphonuclears 35 per cent., lymphocytes 46 per cent.), platelets 46 per cent.

1. HÆMOLYTIC ANÆMIAS.

Since the introduction of recent biochemical tests, it has been possible to separate the anæmias of adults into two classes, viz., those in which there is excessive hæmolysis, and those in which this is not present. This same procedure can be applied to the anæmias of children, and it is necessary to discuss briefly the main features common to hæmolytic anæmias.

In hæmolytic anæmias there is an increase of bile pigment in the blood plasma which stains the skin and the sclerotics a lemon yellow colour. This pigmentation must not be confused with the creamy yellow tint which is often so striking, particularly in the cheeks, the ears and the extremities of children suffering from anæmia of non-hæmolytic origin. Though the spleen is enlarged in the majority of children with anæmia, it is more constant and more striking in the hæmolytic group. In the case of the liver, enlargement is much more likely to occur in the presence of hæmolysis. In contrast to icterus of obstructive origin, the stools of these cases are of normal colour. The urine is usually dark from the presence of excess of urobilin, but very rarely contains bile pigment. It should be remembered that in the early days of life, bile salts and bile pigments are commonly found in the urine as a normal phenomenon. In doubtful cases, van den Bergh's test gives a negative direct and a positive indirect reaction in the plasma, a reaction which varies in intensity with the severity of the hæmolysis. Cases of obstructive jaundice give an immediate direct reaction.

(a) **Pernicious anæmia.** Many writers include as cases of pernicious anæmia any grave anæmia occurring in childhood, and Still[10] even goes so far as to say that 'whether pernicious anæmia as seen in adults ever occurs in childhood is doubtful.' After a careful investigation, we feel convinced that such cases, though rare, are encountered. Notes on one of four such cases which we have personally investigated are given (Case 1), and a further case is described later (Case 7). In all of the four cases the onset was very sudden, the child becoming extremely anæmic within a few days. With suitable treatment recovery was rapid, but the rapidity of onset and recovery is not to be regarded as differentiating the disease from that occurring in adults, but rather as an illustration of the juvenile reaction referred to above.

Case 1. Baby O., aet. 4 months, was admitted to hospital in July 1925 for extreme anæmia, restlessness and dyspnœa. He had been quite fit until a week previously when he was noticed to become pale, and the pallor had rapidly increased without apparent cause. On examination, the mucous membranes were pale and the skin and conjunctivæ tinted a light yellow colour;

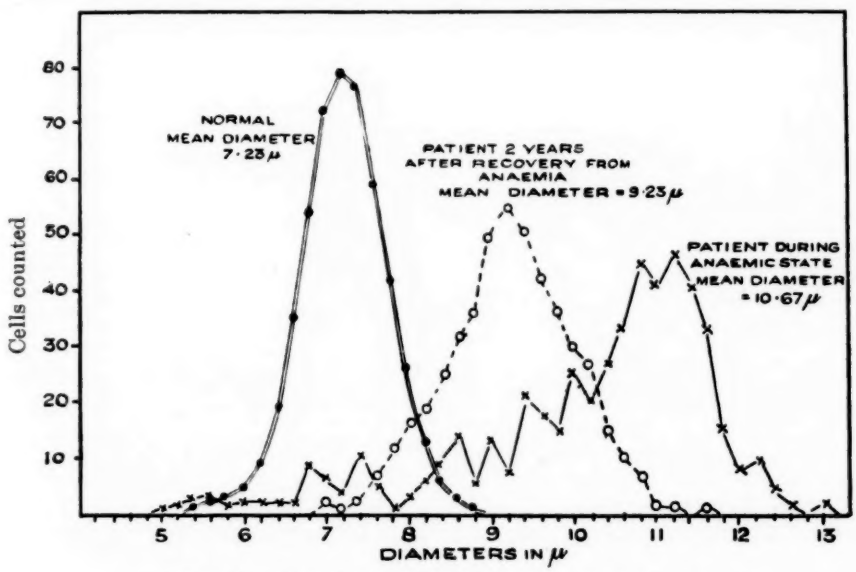

FIG. 7. Diameter of red blood corpuscles in Case 1.

the spleen was palpable ¾ in. below the costal margin: there was a systolic murmur at the apex and there were systolic and diastolic murmurs at the base: the rectal temperature was 100°, pulse 150, respirations 45 per minute. The blood picture showed Hb. 25 per cent.; red cells 900,000; colour index 1·4; white cells 5,300 (polymorphonuclears 27 per cent., lymphocytes 71 per cent., hyalines 2 per cent.). The red cells showed great irregularity in shape and size and the mean diameter was 10·67 μ (normal 7·23 μ). Many cells showed polychromasia, and a few punctate basophilia. The fragility of the red cells was normal and van den Bergh's reaction gave a negative direct and a marked positive indirect reaction. On the morning after admission the hæmoglobin had fallen to 18 per cent. and it was decided to transfuse the patient. Seven ounces of citrated blood were given into the median basilic vein, and immediately there was decided improvement in the child, the distressing dyspnœa was relieved and the pulse rate fell to 120. From this time improvement was uninterrupted: the child has been seen on a number of occasions up to a year ago and there has been no repetition of the anæmia. The only abnormality found has been a constantly increased mean diameter of the red cells (9·23 μ), although the anisocytosis has not been so great. Since the initial attack of anæmia the condition has been similar to that found in adults in the intervals between the hæmolytic crises. Fig. 7 shows the red cell distribution curve on admission and two years later.

(b) Acholuric jaundice.—Occurring in childhood this is almost invariably of the familial type. Thus in 69 members of a family[11] there were 19 known to have had this condition. Of these, 8 were known to have had it before the age of 15 years, 3 died of it before reaching the age of 3 years. The principal features of acholuric jaundice as occurring in childhood are illustrated by Case 2.

Case 2. Allen H. was deeply jaundiced at birth and the urine was dark : this lasted for some weeks. At the age of 6 years he again became jaundiced. Three months after this he contracted diphtheria and this was associated with a recurrence of jaundice. The following year he became anæmic rather suddenly, the pallor being associated with another attack of jaundice. On examination at this time the spleen was palpable 1 in. below the costal margin : Hb. 50 per cent. : van den Bergh's test gave a negative direct and a marked positive indirect reaction. The red cells showed slight hæmolysis in 0·66 per cent. saline solution : the membrane potential of the red cells was 29 millivolts (normal 8 millivolts). The boy's father gave no history of the complaint, but on examination the sclerotics were found to be rather yellow and the spleen was just palpable : his Hb. was 88 per cent., van den Bergh's test gave a very marked positive indirect reaction, and estimation of the fragility of the red cells showed commencing hæmolysis in a solution of NaCl as high as 0·72 per cent. : the membrane potential of the red cells was 18 millivolts.

(c) Hæmolytic anæmias obviously of infective origin.—In the early months of life sepsis of the umbilicus and infection of the alimentary tract are the commonest causes of this group of anæmias : more rarely parasitic infection may be the cause.

(d) Hæmolytic anæmias, congenital or occurring in the early months of life.—Cases of hæmolytic anæmia are not very uncommon in the early months of life. In some the anæmia appears to be due to an exaggeration of the normal hæmolysis encountered after the fifth month of intra-uterine life and which is normally especially marked immediately after birth[12]. When carried to excess, this becomes of pathological significance. In these cases, the red cells and hæmoglobin are reduced at first in approximately the same proportion, but soon the hæmoglobin falls out of proportion to the fall in the number of the red cells (and so the colour index falls) : in the early stages the cells are of remarkably regular size and shape suggesting that the hæmolysis is of primary importance. Later the blood picture changes : the cells becoming much more irregular in shape and size, the anæmia becomes non-hæmolytic in character, and this later stage may be due to a shortage of iron. In support of this view, it is found that the van den Bergh reaction in the earlier stages gives a strong positive indirect reaction, which disappears in the later stages. It is important to note that at no time is the mean diameter of the cells increased. It has already been suggested that the later stage is associated with an iron shortage, and in confirmation of this, administration of iron is often of value. In connection with the earlier hæmolytic phase, it may be noted that in cases of icterus gravis neonatorum in which the fatal issue is postponed, a considerable degree of anæmia is encountered. In another and more severe type the hæmolysis is evident throughout. These cases are often described as ' pernicious ' but they show obvious differences from the true pernicious anæmia described above, and therefore we feel that this term should not be used for this group. A study of these cases suggests that they may be sub-divided into several different groups. In many, the character of the disease suggests an infection, but in

none, either before or after death, has any evidence of this been found. Some of them show an irregular pyrexia, but more often this is only terminal. In nearly all, there is a considerable enlargement of the spleen. Of these severe hæmolytic anæmias, there is one class which is worthy of special mention. It appears to be more common in the months of June to August, and is marked by a sudden onset, the hæmoglobin often falling within 48 hours to a value as low as 20 per cent. Unless immediate treatment is adopted, the child rapidly becomes restless, comatose, and dies. A single adequate transfusion of blood often leads to a recovery almost as dramatic as the onset.

Case 3. S.J., aet. 6 months, was admitted in August, 1926, with a history of having suddenly become anæmic. The child was well nourished, the mucous membranes were pale and the skin and conjunctivæ showed a light yellow colouration. Examination of the blood showed :—Hb. 23 per cent., red cells 1,500,000, colour index 0·77, white cells 12,200 (polymorphonuclears 60 per cent., lymphocytes 32 per cent., hyalines 6 per cent., eosinophils 2 per cent.). There was irregularity in shape and size of the red cells, but the mean diameter was within normal limits, being 7·18 μ. The fragility of the red cells was normal, and van den Bergh's test gave a negative direct and a positive indirect reaction. The child was transfused with 6 oz. of citrated blood, and after this progress though slow was uninterrupted.

In the following case the onset of the hæmolytic crisis was just as sudden, but it is distinguished from the others by the recurrent nature of the attacks.

Case 4. Severe hæmolytic anæmia with splenomegaly, controlled by liver treatment. Sylvia K., aet. one year eight months, was first seen in August, 1928, for severe anæmia and jaundice. There was no family history of any condition resembling this. There was one other child, who was quite healthy. The patient's mother was rather anæmic, and said she had always been so : her hæmoglobin was 74 per cent., and the red and white cell counts and the fragility of the red cells were normal. On physical examination, nothing abnormal could be found, and there was no palpable enlargement of the spleen.

The patient was breast fed until seven months old, and had broncho-pneumonia at seventeen months. She had always had an adequate mixed diet. She had been rather pale since birth, but had been more so for the six weeks prior to being seen. Her mother had noticed that she seemed rather yellow at times, but said she had never been deeply jaundiced. Her bowels were open one to four times daily, and sometimes the fæces were of a rather pale yellow colour, but had never been white.

She was admitted to hospital, and was evidently very anæmic. Her skin had a light yellow pigmentation which also showed slightly in her sclerotics. On systematic examination, her weight was 25 lb. 1 oz., and temperature normal. The whole abdomen was rather distended with gas, the liver was of normal size and consistency ; the spleen was uniformly enlarged and rather firm, extending downwards to the level of the umbilicus. The fæces were normal, and the urine showed no abnormality, there being no bile salts or bile pigments present.

The blood count showed :—Hæmoglobin 32 per cent., red cells 2,060,000, colour index 0·75 : white cells, 9,100 (polymorphonuclears 51·5 per cent., lymphocytes 45·5 per cent., large hyalines 3·0 per cent). There were anisocytosis and some polychromasia. No nucleated red cells or abnormal white cells were seen, and the mean diameter of the red cells was normal.

Other investigations produced the following results :—fragility of red cells in saline solutions normal (hæmolysis commencing in 0·45 per cent. NaCl) ; Wassermann reaction in the blood negative ; urobilin in urine strongly positive ; van den Bergh's reaction in serum negative direct, and strongly positive delayed direct and indirect ; the fæces showed no occult blood or abnormal micro-organisms present.

She improved until November 1st, 1928, on iron ammonium citrate, gr. 5, t.d.s., and the hæmoglobin rose to 60 per cent. On this date she had a hæmolytic crisis, became very anæmic, and the skin and sclerotics became tinted a pale yellow colour. The hæmoglobin dropped to

20 per cent. on November 3rd, and the blood contained many nucleated red cells. On November 6th, the hæmoglobin was 18 per cent. From November 1st to November 6th she ran an irregular temperature up to 101°. She was given three transfusions of blood (total 285 c.cm.) between November 6th and November 12th, when the hæmoglobin was 24 per cent. She was evidently still hæmolysing her red cells at a fast rate.

From November 7th, liver extract equivalent to ¼ lb. of fresh liver was given. On December 3rd the hæmoglobin was 34 per cent. but the patient was still rather yellow: ¼ lb. of fresh liver was then given in addition. On December 26th the hæmoglobin was 42 per cent., and on February 12th, when she was discharged from hospital, the hæmoglobin was 66 per cent., the yellow pigmentation had disappeared and there had been no hæmolytic crisis since the liver extract was started.

She developed whooping cough in March 1929, during which time her mother said she became slightly yellow. Otherwise she has remained perfectly well and has taken the same quantity of liver regularly during the whole time.

On examination on January 27th 1930, at the age of 3 years 2 months, she had gained 8½ lbs. in weight, and looked extremely healthy: the liver was normal, and the spleen had decreased in size so that it was just palpable at the end of a deep breath.

The blood showed:—hæmoglobin 72 per cent., red cells 5,120,000, colour index 0·70: white blood corpuscles 10,600 (polymorphonuclears 55 per cent., lymphocytes 40 per cent., large mononuclear cells 4 per cent., eosinophils 1 per cent.) Anisocytosis and poikilocytosis were within normal limits; the red blood corpuscles of the "ring" appearance; no polychromasia or punctate basiphilia; no nucleated red cells or immature white cells seen; van den Bergh's reaction—direct negative, indirect less than 0·5 units.

The essential feature of this case was a severe hæmolytic jaundice occurring in a child one year old, with an enlarged spleen reaching to the level of the umbilicus: the anæmia and jaundice were not due to Addison's anæmia or to acholuric jaundice. This was controlled by liver treatment, and at the end of nineteen months' treatment, the spleen was only just palpable. The dose of liver necessary to control the abnormal hæmolysis was equivalent to ½ lb. of fresh liver. On half this dose, the hæmoglobin was rising very slowly, and the yellow pigmentation of the skin persisted. The full quantity, which is the full dose normally given to an adult, was taken without any ill effect for fifteen months, and the hæmoglobin rose to a normal value of 72 per cent. The quantity of liver has since been reduced to 2 oz. daily and the patient so far has shown no signs of increasing hæmolysis.

It will be noted that whooping cough was associated with a mild relapse, and we take this opportunity to point out that in many of the cases of hæmolytic anæmia the onset of any acute infection may be associated with a severe hæmolytic crisis. This also applies to the administration of anæsthetics. This association, of course, occurs also in adults, but the reaction in children is usually more severe.

Case 5 is another case of the same nature.

Case 5. Grace B., aged 10 years, was admitted to hospital in March, 1930, on account of severe anæmia and jaundice. There were nine other children in the family, none of whom had ever had this trouble. The father and mother were quite healthy, had no splenic enlargement and the fragility of the red cells was normal in both of them. The patient was said to be rather deeply jaundiced at birth and had been pale since then. She had had about twelve attacks of severe anæmia associated with jaundice: five of these had been very severe and had necessitated admission to hospital. The first severe attack followed measles at the age of eighteen months. The attacks were all similar: in the course of a few hours the child became very feverish, anæmic, and the skin tinted a light yellow colour. In most of the attacks vomiting occurred. On ex-

amination the skin was a lemon yellow colour but the conjunctivæ were very little affected. She was very anæmic ; the spleen was enlarged to one inch below the subcostal plane and was very firm. The liver was not enlarged and the stools were of normal colour. She had a temperature ranging up to 101°. Investigation of the blood showed :—hæmoglobin less than 20 per cent., red blood cells 1,210,000, white blood cells 5,600 (polymorphonuclears 45 per cent., lymphocytes 47 per cent., hyalines 8 per cent.). There were no abnormal forms of red or white cells and the reticulocyte count was 0·4 per cent. van den Bergh's test in the blood serum gave a negative direct reaction, and a positive indirect reaction (2·25 units). The fragility of the red cells was normal. The urine contained no bile pigments, but excess of urobilin. The Wassermann reactions of the child and of her father were negative. The average size of the red cells showed a mean diameter of 6·72 μ (range 5·0 μ to 8·2 μ) as compared with the control average 7·27 μ (range 6·2 μ to 8·8 μ). She was very little improved by blood transfusions of 850 c.cm. as she hæmolysed the blood cells very rapidly. On the equivalent of $\frac{3}{4}$ lb. of liver the reticulocyte count rose to 26·4 per cent. on the 26th day and the hæmoglobin to 32 per cent. Re-examination of the blood on June 25th 1930 showed :—Hb. 52 per cent., red cells 2,630,000, C.I. 1·00, white cells 9,000 (polymorphonuclears 53 per cent., lymphocytes 40 per cent., hyalines 6 per cent., eosinophils 1 per cent.) : van den Bergh's test showed a negative direct and negative indirect reaction (less than 0·5 units). She is still under treatment.

Differential diagnosis of hæmolytic anæmias.

It has already been mentioned that in anæmias of doubtful origin, van den Bergh's test becomes of diagnostic importance in differentiating the hæmolytic anæmias from those of non-hæmolytic origin. For this test, a large quantity of blood is unnecessary. It can be demonstrated satisfactorily by drawing blood from a finger prick into two capillary tubes, using a minute amount of heparin as an anticoagulant. The tubes are sealed and centrifuged : the ends are broken and the cells expelled : the plasma of one is mixed with an equal amount of van den Bergh's reagent, and of the other with an equal part of van den Bergh's reagent and 2½ volumes of alcohol. The mixtures are drawn up into the tubes which are again sealed and centrifuged. The colours of the supernatant fluids are compared with the series of standard solutions in similar capillary tubes.

Red cells.—While in non-hæmolytic anæmias the hæmoglobin is fairly uniformly distributed in the red cells, in hæmolytic anæmias 'shadow cells' are common. In fact, these 'shadow cells' are more common than in adults because the hæmolytic crises are more sudden. Polychromasia, punctate basophilia and nucleated red cells are present in many anæmias, and are not of diagnostic value.

Size and shape of red cells.—In true pernicious anæmia, in children as in adults, there are marked poikilocytosis and anisocytosis : and the average diameter of the red cells is always raised as illustrated in Fig. 8. The colour index is high and usually above unity. In acholuric jaundice poikilocytosis and anisocytosis may also be present, and the average diameter is considerably less than normal [11] as illustrated in Fig. 8. This has been confirmed by Masters, Zerfas and Mettel[13]. The colour index is usually normal in spite of a considerable degree of anæmia ; it never rises above unity. The explanation of this apparent anomaly is that in acholuric jaundice the red cells are of much greater thickness than in other anæmias, as may be clearly seen by examination of the

cells seen floating on their sides in the hæmocytometer chamber. In the other hæmolytic anæmias the mean diameter of the cells is about normal, and poikilocytosis and anisocytosis not so marked except in the cases mentioned above as occurring in the first few days of life.

An examination of the fragility of the red cells to hypotonic solutions of sodium chloride affords a ready means of diagnosis in cases of acholuric jaundice. For this purpose blood is drawn into a small quantity of a solution of sodium citrate and centrifuged. The plasma is pipetted off, the red cells are washed in 0·90 per cent. NaCl, and the suspension again centrifuged. This process in repeated, the final supernatant fluid being withdrawn as completely as possible. In each of a series of small tubes 2 c.cm. of saline solutions are introduced. The concentrations of these solutions range from 0·30 to 0·84 per cent. with intervals

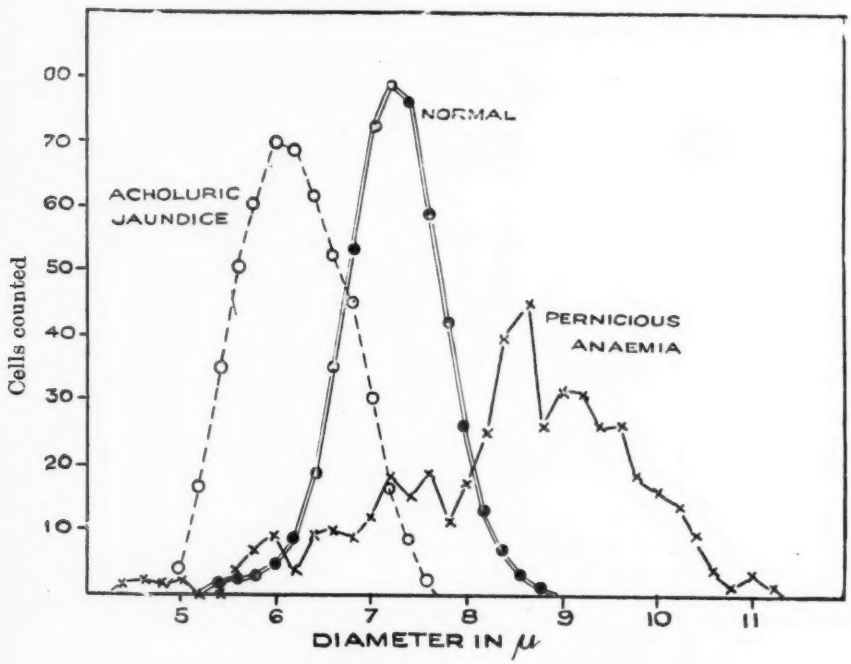

FIG. 8. Comparison of size of red blood corpuscles.

of 0·03 per cent. To each tube 0·1 c.cm. of the washed corpuscles is added and the tubes are inverted several times to ensure even suspension. An equal quantity of corpuscles is similarly added to tubes containing 0·90 per cent. NaCl and distilled water. As a control, the blood of a normal individual should be treated in the same manner. The tubes are allowed to stand for 12 hours : the percentage hæmolysis in each tube is estimated by colorimetric comparison of the supernatant fluids with the 100 per cent. hæmolysis in the tube which contained distilled water. Fig. 9 illustrates curves plotted in a case of acholuric jaundice and in a normal individual. It will be observed that in normal persons slight hæmolysis occurs about 0·48 per cent. but hæmolysis is not quite complete at 0·30 per cent. It is often stated[14] that in solutions weaker than 0·40 per cent. hæmolysis is complete, but when accurate quantitative methods are used

the lower limit is found to be much below this. In acholuric jaundice hæmolysis commences in solutions stronger than 0·48 per cent. ; it has even been observed at 0·84 per cent : and in this disease, hæmolysis is complete in concentrations of NaCl higher than in the normal. In very young children, where large quantities of blood cannot be obtained, the test can easily be performed in a modified manner by allowing a drop of blood to fall into tubes containing 0·51 and 0·48 per cent. NaCl. This gives a ready qualitative method of diagnosis. It is worthy of note that in other hæmolytic anæmias the resistance of the red cells is usually increased and not diminished.

As shown by Hampson and Maizels[15] in cases of pernicious anæmia and acholuric jaundice, the reaction in the red cells is more acid than in the normal. This appears to be associated with a high content of ester phosphate in the red cells and leads to a high potential on the membrane of the cells. This has since been shown to be the case in other varieties of hæmolytic anæmia

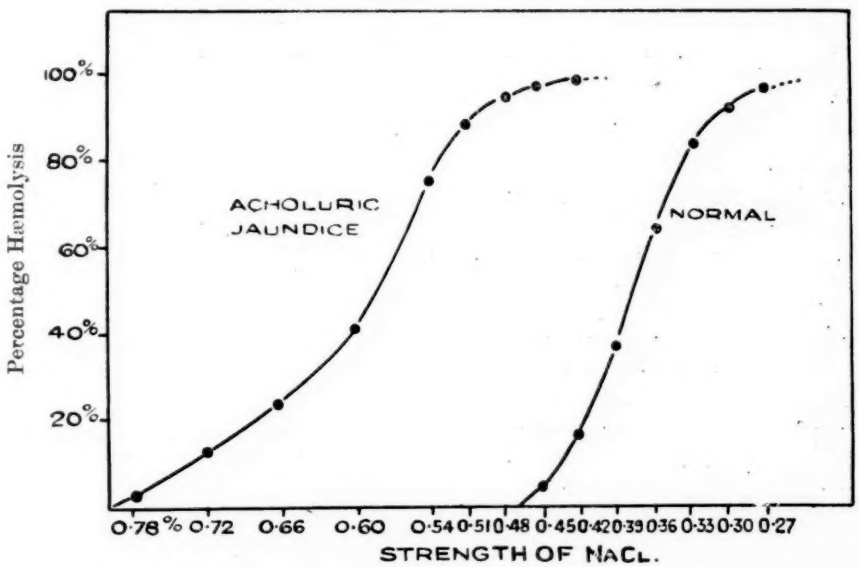

FIG. 9. Fragility of red blood corpuscles in saline solutions.

(as for example in Case 4 where on Nov. 6th a value of 40 millivolts was found). It has not been found in other conditions: in cirrhosis of the liver, for example, a positive indirect van den Bergh's reaction is found, but the electrical charge (or membrane potential) of the red cells is normal (Case 6).

Case 6. Peter B., æt 12 years, had been subject to bilious attacks, occurring about once a month, for about as long as he could remember. He had had two operations at four months' interval for bilateral undescended testicle at the age of 10. Following the first operation, in November 1927, he became slightly jaundiced for 2 days. In September, 1928, he was again jaundiced for three weeks, this time accompanied by abdominal pain and vomiting. In February 1929, he had a sore throat. Two weeks later he was again noticed to be jaundiced : with the onset of the jaundice he had an attack of vomiting and the jaundice lasted a week. At this time he was admitted to hospital. On enquiry, he stated that although the jaundice became more marked in February 1929, he did not think the yellow colour had ever quite cleared since September 1928. On examination, the liver edge was just palpable and the spleen could be felt for about two fingers' breadths below the costal margin. The sclerotics were tinged with yellow

The urine contained a slight excess of urobilin: the Wassermann reaction was negative: van den Bergh's test gave a positive indirect (12 units) but a negative direct reaction; the fragility of the red cells to hypotonic saline solutions was normal: the membrane potential and the phosphate content of the red cells was normal: hæmoglobin was 86 per cent., red cells 4,452,000, colour index 0·94, white cells 7,200—polymorphonuclears 62 per cent., lymphocytes 31 per cent., hyalines 5 per cent., eosinophils 2 per cent.; the red cells were normal in size and shape. Between April 1929 and 1st February 1930, he had periodical attacks of nausea and vomiting; in three of these attacks the jaundice was noticed to increase in intensity. The liver now extended 1½ in. below the costal margin, while the size of the spleen appeared to be the same. Examination of the blood as regards van den Bergh's reaction, fragility, and phosphate content gave similar results to those obtained in February 1929. The Hb. was now 70 per cent. A lævulose tolerance test gave the following results:—blood sugar fasting 0·118 per cent., one hour after 50 grammes lævulose 0·130 per cent., after two hours 0·130 per cent. He was treated with mercury inunctions and was given glucose by the mouth, with injections of insulin. On the 7th March the hæmoglobin rose to 85 per cent., van den Bergh's test became negative, the liver showed slight decrease in size, and a lævulose tolerance test gave the following results:—blood sugar fasting 0·102 per cent., one hour after 50 gms. lævulose 0·110 per cent., two hours 0·110 per cent.

White cells in hæmolytic anæmias.—In true pernicious anæmia it is usual to find a low white count with a relative lymphocytosis. This is also true in grave anæmias of infective origin. In the other types, a high white count is more commonly encountered, and on the whole the presence of this is associated with a better prognosis. In all severe anæmias of the types under consideration, there is a tendency for immature white cells to be found: this is especially the case when the white count is high and is more constant in very young children. It is probably to be regarded as another example of the reaction of the infant's hæmopoietic system to stimulation. As pointed out already, as compared with adults, the percentage of lymphocytes is high in the normal infant, and in older children almost any stimulus to the formation of white cells results in a reversion to the infantile type of reaction and so to a lymphocytosis. Very rarely in this group of anæmias does the lymphocytosis exceed 65—70 per cent., a point of considerable importance in diagnosis, to which reference will again be made.

Treatment of hæmolytic anæmias.

Liver therapy.—Following the work of Minot and Murphy showing the value of the therapeutic administration of liver and extracts prepared from it in cases of pernicious anæmia, it has now become a generally recognized form of treatment for this disease. The application of this in infancy and childhood appears to have been neglected, but as is shown by the following case it is of equal value in true pernicious anæmia even in early infancy.

Case 7. Rose S., had pneumonia at the age of 8 months, since when she had been noticed to be slightly yellow. One month later it was noted that she was becoming anæmic. At the age of 11 months she was brought to hospital. The skin and conjunctivæ were then distinctly yellow, and the mucous membranes were pale. The spleen was palpable three fingers' breadths below the costal margin. No other abnormality was detected on physical examination. The urine contained an excess of urobilin. Examination of the blood gave the following results:—Hb. 37 per cent.; red cells 1,800,000; colour index 1·06; white cells 7,600 (polymorphonuclears 42 per cent., lymphocytes 53 per cent., hyalines 1·5 per cent., eosinophils 0·5 per cent., myelocytes 3 per cent.). There were marked anisocytosis and poikilocytosis, the mean diameter of the red cells was 8·7 μ. Normoblasts were fairly numerous and occasional megaloblasts were present.

van den Bergh's test gave a negative direct and a positive indirect reaction. The fragility of the red cells was normal. A test-meal showed the absence of free HCl in the resting juice and one hour after a feed. The Wassermann reaction was negative. The baby was given liver extract and a fortnight later the hæmoglobin had risen to 54 per cent., and anisocytosis and poikilocytosis were less marked. van den Bergh's test was negative. A month after treatment was first commenced the blood picture was—Hb. 70 per cent.: red cells 3,900,000: colour index 0·9; white cells 6,200 (polymorphonuclears 40 per cent., lymphocytes 57 per cent., hyalines 2 per cent., myelocytes 1 per cent.): van den Bergh's test was negative and no abnormality was detected in the urine.

Although the administration of liver is still common in many anæmias in adults, in the majority of cases the results are totally unsatisfactory, and apart from pernicious anæmia no clear idea appears to exist as to when it is likely to be of value. The following remarks, based on investigations on anæmias occurring in adults are introduced into this paper with the object of showing the application of the knowledge so gained to the anæmias of infancy and childhood. In 1927 it was shown by Hampson and Maizels[15] that in both pernicious anæmia and acholuric jaundice there is an increased electrical charge on the membrane of the red cells, and this was shown to be proportional to the degree of hæmolysis as measured by van den Bergh's reaction. On investigating the effects of the administration of liver in such cases, it has been found that proportional to the decrease in hæmolysis the electrical charge becomes normal. This is illustrated by the values obtained in a patient and shown in the following table :—

	van den Bergh's reaction in units	Membrane potential in millivolts
Before liver feeding	5	27
One week after liver feeding	4	23
Three weeks ,, ,, ,, ...	1	12
Ten weeks ,, ,, ,, ...	0·5	8

In a large series of cases of anæmia of many different varieties, the only cases which have materially benefited by the administration of liver have been those in which there has been a raised electrical charge. Practically all such cases have shown evidence of increased hæmolysis.

From these results it appeared worth while to try the effect of liver feeding in cases of hæmolytic anæmia occurring in childhood, and we are convinced that it is of considerable value in these cases even when the condition is not that of pernicious anæmia. The response in a case of acholuric jaundice is illustrated by the following case.

Case 8. George A. The child was admitted in 1922 at the age of 1 year and 6 months for anæmia. The abdomen was large and the spleen extended below the umbilicus. There was slight beading of the ribs with no other evidence of rickets. The onset of the anæmia had been gradual, but on admission to hospital, the blood showed Hb. 23 per cent., red cells 1,300,000; colour index 0·9; normoblasts were numerous and a few megaloblasts were seen. There was much poikilocytosis and polychromasia. White cells were 30,000 per cubic mm.—polymorphonuclears 21 per cent., lymphocytes 70 per cent., hyalines 3 per cent., myelocytes 6 per cent. During the next two years, the child showed gradual improvement and the case was diagnosed as von Jaksch's anæmia. In 1922 the child had slight jaundice and further examination of the blood showed

marked increase in fragility of the red cells (Fig. 9) and the cells themselves were small in diameter (Fig. 10), and showed the typical dumb-bell shape of acholuric jaundice. Between 1922 and 1928 there were numerous recurrences of anæmia accompanied by icterus, and the liver gradually increased in size. In 1928 it was found that the membrane potential and the phosphate content of the red cells were high. He was given liver extract and the hæmoglobin rose rapidly to 80 per cent., following a sharp rise in the reticulocyte count. The membrane potential and phosphate content of the red cells became approximately normal, and there was some increase in the resistance of the red cells—whereas formerly on numerous occasions laking had commenced at 0·76 per cent. NaCl, laking now commenced at 0·66 per cent. NaCl. After discharge the patient was instructed to take liver regularly. This he failed to do, and as there appeared no likelihood of the régime being effectively carried out, splenectomy was performed. Although the anæmic state persisted at intervals during the seven years the child was under observation, the appearance of the blood film gradually changed. White cells became less numerous, myelocytes disappeared, the differential count became more normal, and nucleated red cells were only found on rare occasions.

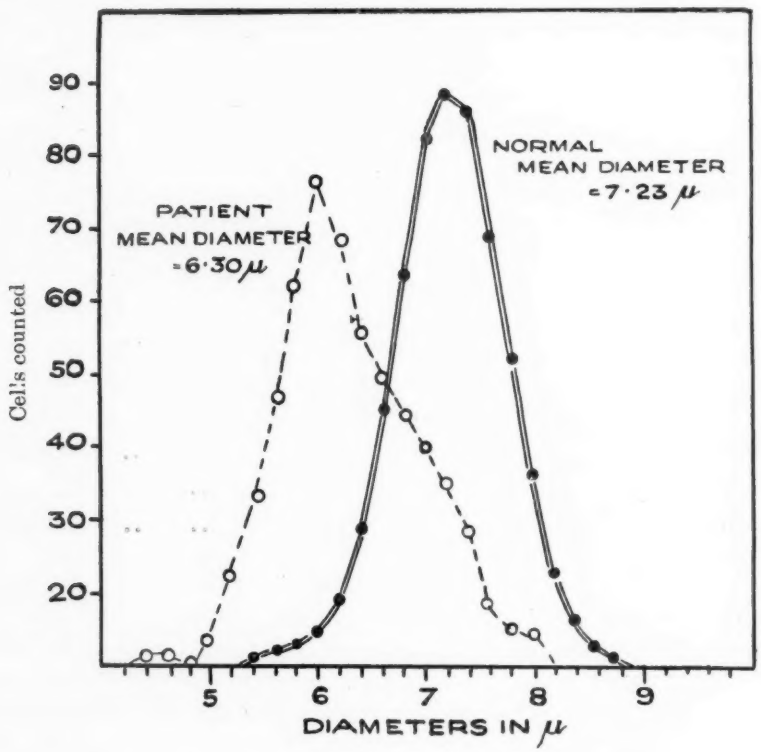

FIG. 10. Size of red blood corpuscles in a case of acholuric jaundice (Case 8).

Case 4, quoted above, showed hæmolytic crises occurring at an early age. This was neither a case of pernicious anæmia nor acholuric jaundice, but the electrical charge (40 millivolts) was the highest we have met. The value of liver therapy in this case was most striking. We have been impressed by the fact that in order to control hæmolysis in children, it is necessary to give a dose of liver which is relatively greatly in excess of the amount required by an adult. Doubtless this is partly to be explained by the greater demands on the hæmopoietic system in a growing child; thus in Case 4, the dose of liver necessary to control the hæmolysis was equivalent to ½ lb. of fresh liver. On half this dose the hæmoglobin percentage was rising very slowly, and the yellow pig-

mentation of the skin persisted. The full quantity, which is the full dose normally given to an adult, was taken from the age of 1 year and 11 months for 15 months and the hæmoglobin value rose to 72 per cent.—a normal value for this age. Again, in Case 5 the equivalent of ½ lb. of liver only partially controlled the hæmolysis, but ¾ lb. did so completely.

The initial fall of hæmoglobin in the hæmolytic crises in children is often of great severity (Cases 1, 4, 5 and 7). The beneficial effects of liver therapy do not become apparent until after the elapse of at least a week, and it becomes of vital importance to tide the patient over this period : it is here that blood tranfusion becomes of special benefit.

The beneficial effects of splenectomy in cases of acholuric jaundice are now well recognized. Although after splenectomy the resistance of the red blood cells to hypotonic saline solutions is increased, it is certainly not our experience that the fragility ever becomes normal[16] as it sometimes stated[14]. This is confirmed by Masters, Zerfas and Mettel[13]. In infancy splenectomy is an operation attended by a very high mortality. The administration of liver extract during this early period of life may tide the patient over to a later age when, if thought advisable, splenectomy can be performed in comparative safety.

Blood transfusion.—In selected cases we are firmly convinced of the efficacy of blood transfusion. In children as in adults it is just as essential that great care should be taken over the correct grouping of the donor and recipient, and it may be necessary to allow corpuscles of an infant to stand with the sera for half an hour, as agglutination may be delayed. It is always our practice to give the transfused blood into one of the peripheral veins such as those in the antecubital fossa and not into the superior longitudinal sinus. We have seen three fatalities following the latter procedure. As this is a method which has been in common use we would emphasize that it is a simple process to withdraw blood from the sinus, but this cannot be taken as proof that the bevel of the needle lies entirely within the sinus : and in delivering blood, part may be delivered into the lumen of the sinus and part into the meningeal spaces.

In most severe cases of hæmolytic anæmia of the infective type, we consider blood transfusion of great value, and in the type which has been described as occurring with sudden onset particularly in the summer months, a single transfusion may be all that is necessary. It has already been remarked that in cases where liver therapy has been adopted, it may be necessary to give an initial transfusion.

In delivering blood into a vein in the antecubital fossa, the process is of necessity slow, and this gives an opportunity for watching the pulse rate and for any signs of cardiac dilatation. It is therefore possible to give relatively large transfusions, and provided the process is carefully watched the results appear fully to warrant them in preference to small transfusions. On several occasions we have given 200 c.cms. to a child only a few weeks old.

In addition to special treatment, attention to the usual hygienic measures is of course essential. Even in the normal infant the reserve of iron is low, and it is therefore important to attempt to remedy this deficiency by the administration of suitable iron salts.

II. NON-HÆMOLYTIC ANÆMIAS.

(a) **Anæmia due to hæmorrhage.**—As compared with adults hæmorrhage is a relatively rare cause of anæmia in infancy and childhood, but when bleeding does occur the loss of comparatively small quantities may readily endanger life. It is encountered in the early days of life in the form of melæna neonatorum.

Case 9. Eliz. B. was admitted to hospital at the age of seventeen days on account of abdominal pain. The child had been seized with sudden abdominal colic and became very blanched. She then started to vomit large quantities of partly altered blood and to pass large quantities of blood per rectum. The abdomen became very distended and in spite of treatment she succumbed within 18 hours of the first symptoms. Post mortem the whole of the stomach and intestines were tremendously distended with blood which originated from profuse oozing of the whole alimentary tract.

It is also met with in hæmorrhage from the umbilical cord, usually associated with sepsis. Very rarely in rather older children hæmorrhage from the gastro-intestinal tract may be due to duodenal ulceration.

Case 10. James W., æt. 6 months, was admitted on account of vomiting, and the first vomit after admission contained a large amount of partially altered blood. He died quite shortly afterwards. Post mortem the child was wasted and the thymus unduly large. The stomach was distended and contained mucus and blood. The intestines contained a large amount of blood. Just distal to the pylorus there was a duodenal ulcer with a ruptured vessel in the base of the ulcer which had been the cause of the hæmorrhage.

HÆMOPHILIA. This cause of bleeding may be met at all ages. In some cases it is readily recognized by the family history, but in others this may be obscured owing to the disease having missed two or three generations. Occasionally sporadic cases occur, and atypical cases may be met with in females as well as in males as is illustrated by the following case.

Case 11. Jean P., æt. 12 months, was admitted in June, 1929, for bleeding from the socket of an extracted tooth. The bleeding had been profuse and on admission the hæmoglobin was 18 per cent. Numerous red cells showed diffuse basophilia: the white cells were 19,400—polymorphonuclears 53 per cent., lymphocytes 26·5 per cent., hyalines 12 per cent., eosinophils 1·5 per cent., basophils 1·5 per cent., myelocytes 2·5 per cent., transitional cells 3 per cent. The blood platelets were numerous. A fortnight later the hæmoglobin had risen to 38 per cent.; the red cells were 2,800,000: the white count had fallen to 5,000—polymorphonuclears 37 per cent., lymphocytes 51 per cent., hyalines 11 per cent., eosinophils 1 per cent., and no abnormal cells were present. In December, 1929, she was readmitted for intractable hæmorrhage from her lip which had been cut 14 days previously. In the interval the child was said to have regained her normal colour. This time the hæmoglobin was 40 per cent., white cells 18,500—polymorphonuclears 40 per cent., lymphocytes 56 per cent., hyalines 2 per cent., eosinophils 1 per cent., basophils 1 per cent. The blood platelets were 220,000, and the blood calcium 9·8 mgrm. per cent. Both bleeding and clotting times were very much prolonged. On enquiry it was found that there was rather profuse hæmorrhage from the cord after birth and that the child had always bruised very readily. There was no history of any similar condition in the family.

There are instances in which this condition has led to bleeding from the umbilical cord which may be of alarming extent or even fatal. Such a family is illustrated in Case 12.

Case 12. Jack L. was admitted for a hæmatoma in the left thigh. He had had three previous attacks of hæmorrhage in the same position. At the age of eighteen months he had bleeding from the gums and at the age of four a severe epistaxis. He had always bruised very easily and very frequently suffered from painful swellings under the skin following slight injuries.

Although the parents did not give a history of abnormal bleeding two other children had died from bleeding from the umbilical cord at birth. Investigation showed: Hb. 74 per cent., red cells 4,320,000, white cells 9,100, differential count normal, blood platelets 170,000 per c.mm., blood calcium 9·37 mgrm. per cent., and bleeding and clotting times 3 days after admission within normal limits.

This case illustrates the fact that if the blood be examined repeatedly there are periods between the attacks of hæmorrhage when the clotting time may be normal, whereas during the attacks this may be very delayed and at such times trivial injuries may lead to serious hæmorrhage. Some closely allied cases show a lowered platelet count in addition to the typical characters of hæmophilia. Although in many of these cases the hæmorrhage is subcutaneous and of small extent, when there is an open wound (even with dental extraction) the amount of hæmorrhage may be serious.

PURPURA.—In this paper we are only concerned with anæmia occurring in infancy and childhood, and purpura as a cause of anæmia during this period is rare. The anæmia is usually secondary to hæmorrhage from the nose, kidneys or intestines. There may be purpuric spots scattered over the body especially on the limbs, though if the patient has been kept in a recumbent position the petechiæ may be more evident in the sacral region and over the buttocks. Troublesome bleeding sometimes occurs from the gums and may suggest scurvy. During the attacks some degree of pyrexia is often encountered, and in a case of renal bleeding the pyrexia with hæmaturia and the presence of blood-casts in the urine present a picture strongly suggestive of acute nephritis. Often, too, there is albumen in the urine somewhat in excess of the amount of blood. During the attacks there is a low platelet count and the spleen may be enlarged, though this is not invariable. Considerably reduced platelet counts may be found in cases of aplastic anæmia and in leukæmia, and when hæmorrhages occur in these conditions the diagnosis may be difficult. Reference to this will be made again when these conditions are under discussion.

Case 13 is an example of purpura occurring in a child ten years old.

Case 13. Grace D., æt. 10, gave a history of repeated epistaxis and bleeding from the gums for six weeks. Although the epistaxis had been most marked during this time, for some years there had been a tendency to slight bleeding from the nose. On examination the child was very pale: petechiæ were scattered over the body but were most marked on the lower limbs, except that after the blood pressure had been taken, a crop of petechiæ occurred below the area of compression by the arm-band. Slight pressure on the gums produced bleeding which continued for hours, and purpuric spots were present on the tonsils, but otherwise the tonsils were not abnormal: the temperature on a few occasions reached 99°, but otherwise was normal: the spleen was palpable one inch below the costal margin. Examination of the blood showed: Hb. 30 per cent., red cells 2,900,000, colour index 0·52: white cells 4,900—polymorphonuclears 59 per cent., lymphocytes 41 per cent.: platelets 90,000: coagulation time 1′ 40″(Dale and Laidlaw): bleeding time much prolonged: van den Bergh's test negative. Transfusion of blood followed by splenectomy led to almost immediate cessation of bleeding. On the day after splenectomy the patient was again transfused, and thereafter recovery was uninterrupted.

Although in the majority of cases of thrombocytopenic purpura the results of splenectomy are very satisfactory, it appears to us that the cases in which there is a family history belong to a different group. In our experience of these cases the platelet count does not rise after operation, with the consequence that

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the bleeding continues into the peritoneum and in the abdominal wall, and the results have been invariably fatal within a few hours, in spite of transfusion.

(b) **Chlorotic anæmias.**—Anæmias of the chlorotic type are by no means uncommon. As with the true chlorosis occurring in the adolescent female, so in childhood, the cause may be very difficult to find. The anæmia with low colour index is perhaps due to a variety of causes such as prematurity, diet insufficiencies, unhygienic conditions, minor infections, overwork and lack of sleep. It has been described by various writers as due to each of these conditions. In severe cases the child presents a peculiarly white waxy appearance, which is in marked contrast with the yellowish colour of the skin found in so many anæmias in young people. Although gain in weight is unsatisfactory the child appears well covered, probably due to an excess of water in the tissues. An examination of the blood shows a fall in the hæmoglobin greater than the reduction of the red cells, and consequently a low colour index. The hæmoglobin may fall to below 20 per cent. While a fatal termination to the anæmia is rare, the resistance of the patients to infections is impaired and they may succumb to some intercurrent condition which would not be considered grave in otherwise healthy children. It is perhaps of interest here to note that in anæmic adults it is fairly common to obtain a history of anæmia of the chlorotic type occurring in early life. In a study of infants attending out-patient departments and welfare centres, Helen Mackay came to the conclusion that some degree of anæmia was the rule in children under the age of two. The anæmia she described was improved in almost every case by the administration of iron. She pointed out the importance of early treatment in these cases. Shortage of iron is undoubtedly an extremely important factor in chlorotic anæmias; and where the food has contained only traces of iron, an anæmia insidious in onset may become extremely marked. In a case recently seen by one of us, a child had been fed on the breast without supplementary feeding for 2½ years. The value of the hæmoglobin was 22 per cent. Dietetic treatment with the administration of iron led to rapid improvement. Transfusion is usually neither necessary nor desirable unless there is some accompanying infection which renders a rapid rise of hæmoglobin almost imperative. Failure to respond to treatment is almost always due to insufficient dosage of iron. Relatively large amounts are necessary. For the first few days the dose should be increased gradually or somewhat troublesome alimentary symptoms may present themselves, but after this, large doses are almost always well tolerated. In agreement with the findings of Helen Mackay, in our opinion iron ammonium citrate is the best form for administration, and leads to the most rapid improvement (up to 20 grains being given per diem at the age of one year).

Case 14. Eric P., æt. 4 months, was admitted on January 31st, 1930, for severe anæmia. At birth the weight was 4 lb. 3 oz., and he had been fed on dried milk with the addition of cod liver oil. He had always been pale: there had been no hæmorrhage. On admission he was extremely anæmic and of a pale waxen colour. Blood examination showed: Hb. 35 per cent., red cells 3,400,000, C.I. 0·51, white cells 7,000 (polymorphonuclears 34·5 per cent., lymphocytes 48·5 per cent., hyalines 12·5 per cent., eosinophils 4·0 per cent., basophils 0·5 per cent.) There were no abnormal red or white cells present. He was given saccharated carbonate of iron in one-grain doses, thrice daily: the hæmoglobin was only 40 per cent. on March

4th, 1930. The dose of ferri carb. sacch. was then raised gradually to 10 gr., t.d.s., and in spite of an intercurrent attack of measles, on May 28th, 1930, the hæmoglobin was 63 per cent.

In the paper referred to above, Helen Mackay noted that in a group of cases with rachitic manifestations, the hæmoglobin values were approximately the same as in those without rickets. In older children we are of the opinion that rickets is associated with a fall in the value of the hæmoglobin.

Anæmia of a similar type may be found in association with other diseases—as, for example, in coeliac disease.

(c) **Grave secondary (aplastic) anæmias.**—There is a group of anæmias which although rare in early childhood becomes increasingly common in older children. Similar cases occur in adults, and now that pernicious anæmia in adults has become sharply defined, and in the majority of cases responds so readily to liver therapy, the cases under consideration have shown themselves to be of an obviously different nature. We wish to stress this because the literature on the subject is very confusing. In the past, various authorities have grouped these cases with the hæmolytic anæmia described by Addison as pernicious. Writing on this subject, Poynton, Thursfield and Paterson[14] say, 'although writers have insisted upon the wide differences between anæmia gravis in childhood and pernicious anæmia in the adult, we are inclined to think that the essential resemblance is much more convincing, and to believe that the differences do not lie so much in the nature of the disease as in the fact that we are dealing in the one case with an adult, and in the other with a child.' We have already drawn attention to differences in reaction between adults and children (most marked, of course, in infancy) but we do not think that the condition under discussion is an example of such reaction. We agree with the above writers when they say, 'it is certain that most of the cases reported under this heading (pernicious anæmia) are examples of other forms of severe anæmia'; but we feel convinced that true pernicious anæmia does occur in very young children and cases of this disease, fully investigated, have been recorded above. In these cases, the picture showed a remarkable resemblance to the disease as it occurs in adults, and contrasts strongly with the 'anæmia gravis' at present under consideration. Moreover, the anæmia gravis has its counterpart in the adult in a form similar to that found in children, and very different from true pernicious anæmia. Probably this group is a composite one, but apart from the fact that spontaneous improvement occurs in occasional cases, they are all entitled to the name of grave anæmia in that treatment appears to have very little effect on the course of the disease. General treatment, iron, arsenic, liver therapy, and blood transfusion appear to exert very little influence on the course of the disease—indeed transfusion in some cases appears to lead to an exacerbation of the condition. Many of the cases are said to have been anæmic for years, but the condition has not previously caused anxiety. In a few cases the anæmia appears to have occurred so soon after whooping cough or diphtheria as to suggest a causal relationship. There is often irregular pyrexia and this suggests a possible infective origin, though usually none can be discovered except near the end when it appears probable that the infection may be due to a lowered resistance. A tendency to bleed is common to all

of these cases, though considerable hæmorrhages are rare. Associated with this there is a low platelet count. All the cells of marrow origin are reduced—there is a low red cell count and a low white count, the polymorphonuclears being especially reduced in number. The degree of reduction in white cells and platelets appears to be of prognostic significance. No evidence of increased blood destruction is found post-mortem, Perle's reaction on liver and spleen being negative. The whole picture suggests an aplastic anæmia and post-mortem examination reveals a white marrow. Occasional slight improvements in the blood condition associated with marrow activity are not incompatible with a condition which in the main is aplastic. The diagnosis may offer considerable difficulties. We have seen such cases diagnosed as purpura, but the degree of anæmia is altogether out of proportion to the amount of hæmorrhage when such occurs. In other cases 'aleukæmic leukæmia' has been suggested, but in the condition under consideration the number of immature white cells is always under 1 per cent. The superficial glands are not more enlarged than in many otherwise normal children. Hodgkin's disease may present a very similar clinical picture, and this should always be carefully considered. At times the picture, with anæmia, pyrexia, purpura and splenic enlargement, may closely simulate that of malignant endocarditis. In addition the heart often shows some degree of dilatation: there is a systolic murmur at the apex, and often a diastolic murmur at the base: the latter is frequently harsh in character and may be fairly prolonged; it may often be accentuated by extending the neck or by drawing the chin forward.

Case 15. Joan B., æt. 11, was admitted for anæmia. There was a rather indefinite history of lassitude during the preceding year. During this time there had on several occasions been bleeding from the nose, but not sufficiently severe to account for the anæmia. There had been no sore throats and there was no history pointing to infection. On examination she was found to be extremely pale. There was no yellow coloration of skin or sclerotics. The gums bled easily. The glands were palpable in the neck and the spleen could be felt about one finger's breadth below the costal margin. There were a few scattered purpuric spots and slight œdema over the legs. Systolic and diastolic murmurs could be heard at the base of the heart. Examination of the blood showed a negative reaction to van den Bergh's test: Hb. 23 per cent., red cells 1,200,000, C.I., 0·96: white cells 2,700 (polymorphonuclears 21 per cent., lymphocytes 77 per cent., hyalines 2 per cent.): platelets 120,000. In spite of treatment by transfusion, and by administration of iron and arsenic the patient became more anæmic and died. At autopsy, there was no evidence of endocarditis, the only finding of importance being a white marrow.

The following notes on a case in an adult (Case 16) show that there is no essential difference between the disease in adults and children.

Case 16. Percy J., æt. 27, a glass bottle maker, was admitted to hospital in 1928 for extreme anæmia. In 1912 he had appendicectomy, followed by peritonitis and abscess in the right lung. He made a complete recovery from this. Five weeks previous to admission he had pain in the left shoulder, followed shortly afterwards by pain in the right shoulder. Then he had dyspnœa on exertion, his legs felt weak, and the pallor of his face which had been noticed for the previous 3 years became much more marked. On admission he was extremely anæmic, and had marked purpura on the left arm and shoulder, with a sub-conjunctival hæmorrhage in each eye. There was a soft systolic murmur at the base of the heart, the spleen was not palpable, and blood examination showed: Hb. 19 per cent., red cells 1,040,000, colour index 0·94, white cells 4,200 (lymphocytes 61 per cent., polymorphonuclears 39 per cent.). Other investigations showed: no occult blood in the stools, van den Bergh's reaction negative, Wassermann reaction negative, and the fractional test meal showed acid within normal limits. Later, bleeding from the gums

occurred, and a blood count 6 weeks after admission showed : Hb. 17 per cent., red cells 766,600, white cells 3,222 (lymphocytes 69 per cent., polymorphonuclears 31 per cent.). In spite of two transfusions of blood he died 2 weeks later, and autopsy showed complete absence of hæmopoietic activity in the bone marrow, petechial hæmorrhages on the epicardium and pleura, and diffuse fatty degeneration of the heart.

(d) **Splenic anæmia.**—Considerable enlargement of the spleen is often associated with anæmia in children, but very few of these cases are examples of true splenic anæmia. Many writers deny the occurrence of the disease in childhood, but on enquiring carefully into the history in adults, it is not uncommonly found that anæmia has been present during childhood. We are of the opinion that the disease may be diagnosed at an early age. Points especially to be noticed in clinical diagnosis are the firmness of the spleen, the occasional occurrence of small hæmatemeses, and the slowly progressive character of the anæmia. In the later stages the liver becomes involved, with cirrhosis and portal obstruction. The blood picture shows a low hæmoglobin value and a low colour index. The red cells are pale ; there is moderate anisocytosis and the mean diameter is not raised. The fragility of the red cells is not increased, and in the later stages when cirrhosis is present may actually be diminished. There is usually leucopenia with a relative lymphocytosis. There is only a slight increase in the amount of bilirubin in the blood as shown by an indirect reaction to van den Bergh's test, unless the liver is severely damaged. The platelet count in this condition is usually low, but in a condition presenting closely similar features is high. In this latter type, thrombosis is common in the veins of the portal system, and associated with this a transient ascites occurs at an early stage. Case 17 illustrates the features in an advanced case.

Case 17. J.F., æt. 9, was admitted on May 21st, 1929, for abdominal enlargement and drowsiness. The parents and six other children were alive and well. He had measles when four and diphtheria recently, having been discharged from a fever hospital on May 12th 1929. The abdomen had always been rather large but became much more so while he was in the fever hospital. The doctor there found ascites and splenomegaly, and during the latter part of his stay he had hæmaturia as well. This had persisted but had become much less up to the time of his being seen by one of us. There was no history of any hæmaturia before the diphtheria. On examination he was distinctly drowsy, the abdomen was much distended and the abdominal wall tense (circumference at umbilicus 32½ inches). The distension was due to fluid as there was a marked fluid thrill and shifting dullness ; on dipping through this an enlarged spleen could be felt reaching nearly to the umbilicus. On deep palpation a very small and very hard liver could be felt extending just below the xiphisternum. It was evidently cirrhotic. Examination of the chest showed markedly distended veins extending up from the abdomen, and there were signs of fluid at the bases of both lungs. This was confirmed by X-ray examination, which also showed a very large heart shadow suggesting some pericardial effusion. The urine showed the presence of blood and albumen : the amount of albumen was not in excess of that due to the blood. Microscopically, red cells but no casts were seen. There was slight œdema of the legs, and the blood pressure was 140 mm. systolic and 105 mm. diastolic. At no time was there any pyrexia. Investigations showed : Hb. 62 per cent., red cells 3,487,000, C.I. 0·89, white cells 4,000 (polymorphonuclears 85 per cent., lymphocytes 10 per cent., hyalines 4 per cent., and eosinophils 1 per cent.). No abnormal forms of red or white cells were seen. Platelets 160,000 per c.mm. A little ascitic fluid was withdrawn for examination, and showed some blood (? contamination) and 530 leucocytes—mainly lymphocytes—per c.mm. The protein content was 0·8 per cent. The Wassermann reaction in the blood and the ascitic fluid gave negative results. On June 1st 1929, the liver tolerance test after 30 grm. of lævulose showed blood sugar

values of :—fasting 0·105 per cent., ¾ hour later 0·173 per cent., at 1½ hours 0·120 per cent., at 2¼ hours 0·114 per cent., an extreme degree of liver deficiency. The fæces contained no occult blood. A diagnosis of splenic anæmia with cirrhosis of the liver (Banti's disease) was made. With complete rest in bed on an ordinary diet with the addition of as much glucose as he could take, the general condition of the patient improved, and the blood disappeared from his urine. The ascitic fluid was absorbed almost completely, so that on June 20th 1929, the abdominal girth was 25½ inches. On July 1st, 1929, Mr. R. C. B. Ledlie operated on the patient, and in view of his previously serious condition, it was decided not to perform splenectomy, but to tie the splenic veins instead. Mr. Ledlie confirmed the diagnosis and found a very large, hard spleen and a small cirrhotic liver. He was able to tie at least 9–10ths of the splenic veins, the only difficulty throughout being the bleeding from the enlarged vessels in the anterior abdominal wall and the gastro-splenic omentum. The patient made a rapid recovery from this operation : there was a little coffee ground vomit on July 4th 1929, and also epistaxis. The blood reappeared in the urine for six days and then finally disappeared. The spleen temporarily enlarged to the level of the umbilicus. Recovery was otherwise uneventful. On July 8th 1929, blood examination showed : Hb. 53 per cent., red cells 3,125,000, C.I. 0·86 ; white cells 6,250 (polymorphonuclears 73 per cent., lymphocytes 16 per cent., hyalines 11 per cent.); platelets 500,000 per c.mm. There were no abnormal forms of red or white cells present. On July 13th, the platelets were 870,000. On readmission on September 16th 1929, he looked the picture of health, was very active and had gained 5 lb. in weight. There was no sign of any fluid in the abdomen. The lower margin of the spleen was now 1 inch above the umbilical level, and the liver felt unchanged. Blood examination showed : Hb. 84 per cent., red cells 5,100,000, C.I., 0·82 ; white cells 6,400 (polymorphonuclears 73 per cent., lymphocytes 21 per cent., hyalines 4 per cent., eosinophils and basophils 1 per cent. of each) : platelet count, 350,000 : the liver tolerance test with 50 gms. of lævulose showed resting 0·104 per cent., ½ hr. later, 0·118 per cent., 1 hr. later, 0·116 per cent., 1½ hrs. later 0·106 per cent.,—a normal result.

Re-examination on 12th May, 1930, showed that the patient had gained 7 lb. in weight, and he looked extremely well. There was no fluid in the abdomen, the veins on the abdominal wall were very much smaller, and the liver and spleen had remained unchanged. The blood showed :—Hb. 60 per cent., red cells 4,980,000, white cells 6,300 (polymorphonuclears 60 per cent., lymphocytes 29 per cent., hyalines 8 per cent., eosinophils 2 per cent., basophils 1 per cent.) : platelets 337,000. The blood sugar before 50 grm. of lævulose was 0·110 per cent., ½ hour after was 0·129 per cent., 1 hour after 0·137 per cent., and 1½ hours after was 0·137 per cent.

It may be difficult to differentiate splenic anæmia from biliary cirrhosis especially when this is of the type described by Gilbert and Fournier[17], in which enlargement of the spleen is more marked than that of the liver. In biliary cirrhosis, jaundice occurs in the early stages and is of a remittent character, being usually deeper in each successive attack, and for this reason often presents a similarity to acholuric jaundice rather than to splenic anæmia, though the fragility of the red cells is never increased. In discussing treatment the advisability of splenectomy arises. An effect of splenectomy is to produce a rise in the platelet count, and if before operation the count was normal or high, there is a grave danger of subsequent thrombosis in the portal system, and in our opinion a high platelet count constitutes a definite contra-indication to this procedure. When the count is normal the risk is still considerable. When the platelet count is low, splenectomy in the majority of cases will effect a cure. In young children the operative risk is considerable, and in very slowly progressive cases it may be desirable on this account to postpone operation to a later age. In Case 17, the patient was not considered in a fit condition for splenectomy, but it was felt that as his condition was so serious, some operative procedure with the object of limiting splenic activity was desirable. In the light of the work of R. M. Pearce[18], it seemed that this object might be attained

by ligature of the splenic veins. The operation in this case was found to be simple and was not attended by any severe surgical shock. The clinical results were extremely satisfactory and whereas the liver function as demonstrated by the lævulose tolerance test was grossly impaired before operation, six weeks later a normal result was obtained. It will be noted that as with splenectomy the platelet count rose from a pre-operative figure of 160,000 to 870,000 per c.mm. thirteen days later. It would appear from this that ligature of the splenic veins is only indicated when the platelet count is low. The operation has the great advantage that it is rapidly performed and the dangerous procedure of dividing splenic adhesions is avoided.

(e) **Anæmias associated with metabolic disturbances.**—Perhaps the best known example of this is the anæmia associated with thyroid deficiency. This may be very severe, is accompanied by a low colour index, and usually responds readily to thyroid medication, although it may be advisable in some cases to give iron salts as well.

Less well recognized is the fall in hæmoglobin met with in cases of catarrhal jaundice, although this is seldom sufficiently severe to necessitate treatment. In another group of cases periodic attacks of mild jaundice of hepatic origin are associated with cyclical vomiting, and in these a troublesome degree of anæmia may be encountered. In this condition there is a low colour index, with frequently a moderate leucocytosis.

Clinically the attacks are marked by pyrexia and extreme prostration, and the picture may be very similar to that of leukæmia, a point to which we shall return later. The attacks of jaundice, pyrexia and anæmia also present points of similarity to the biliary cirrhosis referred to above. For treatment, in addition to the well-known effects of administering glucose and allied preparations, it is usually advisable to give adequate doses of a readily assimilated form of iron such as iron ammonium citrate.

Case 18. Joseph B. developed a slight cold at the age of 15 months and was noticed to become pale and restless. A month later he suddenly became much more anæmic. After a few weeks the condition improved and an attempt was made to 'feed the child up' to make up for the period of illness. This was rapidly followed by vomiting, and the child became fretful, pale and restless. A month later there was a further attack of vomiting, again associated with anæmia. After 3 weeks' interval there was yet another attack. In January 1928, the child was seen by one of us, and blood examination showed :—Hb. 32 per cent., red cells 2,100,000, white cells 7,800. The red cells showed anisocytosis and poikilocytosis, but the mean diameter was normal. There was at this time distinct jaundice. Fats were largely omitted from the diet and the amount of sugar was increased : after this there were only one or two mild attacks of vomiting and he fairly rapidly recovered from his anæmia. Two years later he is still in perfect health.

(f) **Anæmias of infective origin.**—It is well known that the acute specific fevers and sepsis are frequently associated with anæmia (Case 19). That occurring in infective endocarditis has already been referred to, though the latter condition is rare in childhood and very rare in infancy.

Case 19. Lilian E., æt. 6 weeks, became jaundiced on the first day after birth, and had become progressively so until admitted to hospital. When 5 days old she had convulsions and when 3 weeks old there was a watery umbilical discharge. On admission the child was deeply

jaundiced, and had large subcutaneous hæmatomata on the face, scalp, and body. She was in a condition of tetany which yielded to injections of calcium chloride. A blood count showed :— Hb. 34 per cent., red cells 1,800,000, colour index 0·94, white cells 22,400, platelets 53,000. The liver was regularly enlarged and was firm : it reached nearly to the level of the umbilicus. van den Bergh's reaction gave a strong positive immediate direct reaction and a positive indirect reaction. The urine contained sugar and albumen, and the blood-sugar value was 0·209 per cent. She improved for a time, the effusions of blood disappeared, the jaundice became less marked, the liver became smaller and the child gained in weight. Later she became weaker and died, and post mortem the umbilical vein was found thrombosed and full of pus, and there were multiple abscesses in the liver which was itself becoming cirrhotic.

In the anæmia associated with diphtheria, myelocytes are not uncommonly found. In Still's disease, there is often a moderate degree of anæmia which is not so severe as the pallor suggests. The enlargement of the spleen and of the glands may at first sight suggest a blood disease but the condition of the joints is diagnostic. Other conditions producing pallor and anæmia are acute rheumatism, particularly with pericarditis or endocarditis, and nephritis. Rarer causes of anæmia of this type are congenital syphilis and tuberculosis : in all these the associated clinical picture is usually so evident as to leave no doubt as to the cause of the anæmia.

(g) Hogdkin's disease, leukæmia, chloroma, and glandular fever.—The presence of glandular enlargement, splenomegaly, recurrent bouts of pyrexia and severe anæmia are so common in childhood as to present considerable difficulties in diagnosis.

In Hodgkin's disease anæmia is not often one of the earliest symptoms. When present it is marked by a low colour index, and the white cells are either increased or decreased according to the stage of the disease. Some cases show eosinophilia, but taken as a whole the blood picture is not diagnostic. The glands are discrete, of elastic consistency, and the enlargement frequently starts in the upper cervical region. In children, moderate enlargement of the spleen is usual. When there is an intermittent pyrexia the glands and the spleen frequently enlarge still further, and then subside with the temperature. The disease is not seldom associated with tuberculosis as illustrated by the following case.

Case 20. Douglas C., æt. 9, since November, 1925, had been noticed to be irritable and had developed a dry cough and nocturnal enuresis. On examination in March 1926, he was distinctly anæmic : Hb. 30 per cent., red cells 2,000,000, C.I. 0·75 ; white cells 5,200 (polymorphonuclears 61 per cent., lymphocytes 31·5 per cent., hyalines 6 per cent., eosinophils 1 per cent., basophils 0·5 per cent.). The spleen was firm and enlarged to the level of the umbilicus, and there was an enlarged tender gland above the right clavicle. There was a well marked water-hammer pulse (B.P. 115/40) and capillary pulsation, but no aortic bruit could be heard. A well marked harsh systolic bruit was heard over the whole præcordium. During the stay in hospital he had intermittent bouts of pyrexia lasting 2 to 3 weeks, and reaching 104° in the rectum for several days at a time. During these bouts the supraclavicular gland and other glands in the neck and axillæ and also the spleen became much larger and more tender, subsiding again with the decline of the temperature. He had a splenic rub and pleural rubs on two or three occasions. During one of the relapses he developed epistaxis and purpura, and died. Post mortem miliary tuberculosis was found in the lungs, and the glands and spleen proved to be typical of Hodgkin's disease. The heart muscle was very fatty but no valvular lesion was found.

Leukæmia is much more common than is generally recognized, and although usually of the lymphocytic variety, may be myelocytic. Its onset may be insidious but much more usually is dramatic and may only be recognized on routine blood examination after excessive hæmorrhage from slight trauma. In three of our cases such hæmorrhage had occurred after extraction of a tooth. Considering the ready tendency of lymphoid tissue to hypertrophy in children it is remarkable that the glands, although numerous, are usually small. Glands of this nature are found in the neck, axillæ and groins and have usually appeared simultaneously in these situations, a point of importance in differentiation from Hodgkin's disease. As in this latter condition, there may be a slight irregular pyrexia, but at intervals this becomes much more pronounced and is associated with further enlargement of the glands, the liver and the spleen, which subsides with the pyrexia. During these phases there is profound prostration and the hæmoglobin falls to a very low level. At such a time blood transfusion may be followed by a remarkable improvement and the hæmoglobin may rise 30 or 40 per cent. The improvement is only temporary, and a fatal issue is not long delayed. This is well illustrated by Cases 21 and 22, and three similar cases are instanced by McLean and Caffey[9].

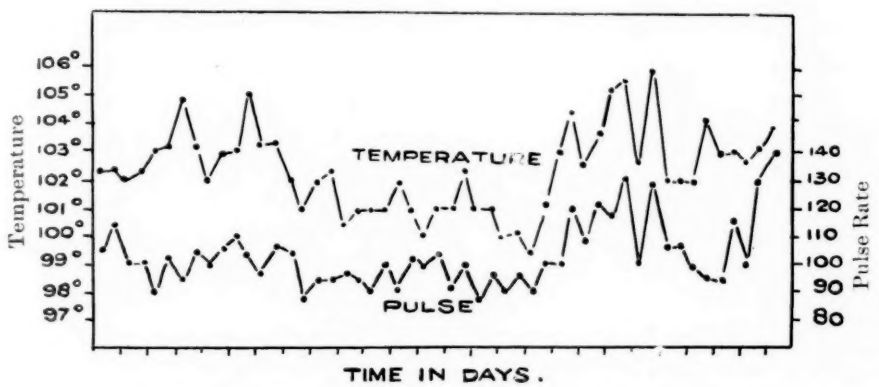

FIG. 11. Temperature and pulse rate in leukæmia (Case 21).

Case 21. John B., æt. 2 years 4 months, was admitted on 9th February, 1930. In September 1929, he had whooping cough of mild type. Since October, 1929, he was noticed to be weak, particularly in his legs, and in December he became irritable, sleepless and unsteady on his feet. He was treated with antipyrin and developed a purpuric rash. On admission he was extremely pale and very irritable and had hæmorrhagic sordes round the mouth; he had slight general enlargement of the glands in the neck, axillæ and groins and the spleen was palpable one inch below the costal margin: there was also moderate enlargement of the liver. Blood examination on the 22nd January, 1930, had shown Hb. 60 per cent., red cells 5,440,000: white cells 24,000 (polymorphonuclears 2·7 per cent., lymphocytes 83 per cent., pro-lymphocytes 14 per cent., eosinophil myelocytes 0·3 per cent.). The red cells showed some anisocytosis and poikilocytosis, and 5,000 nucleated red cells per c.mm. were present. On the 10th February, the Hb. had fallen to 30 per cent., and the red cells to 2,500,000; the white cells numbered 4,000 (polymorphonuclears 2 per cent., lymphocytes 63 per cent., pro-lymphocytes 11 per cent., lymphoblasts 22 per cent., eosinophil myelocytes 1 per cent., basophils 1 per cent.). The blood platelets were very scarce. On 13th February, the Hb. fell to 23 per cent., and on the 15th Feb

ruary 12 oz. of citrated blood were transfused. On 24th February, the Hb. had risen to 65 per cent., and this was maintained until 28th February. The white cells still numbered 4,000 (polymorphonuclears 6 per cent., lymphocytes 62 per cent., pro-lymphocytes 23 per cent., lymphoblasts 7 per cent., hyalines 2 per cent.). During this time the spleen became impalpable, but subsequently became very large again. The Hb. rapidly fell to below 20 per cent. before death ensued. During the whole course of the disease there were periods of irregular pyrexia illustrated by Fig. 11.

Case 22. Margaret D., æt. 3, was admitted on 12th February, 1930, for generalized painful glandular enlargement and anæmia. In December, 1929, there was pain in the right arm with inability to use it. At this time enlarged glands on the right side of the neck were first noticed. Later the left thigh and knee became painful and tender to touch. A series of pyrexial attacks occurred each lasting three to five days, with intervals between, which, occasionally were as long as sixteen days. During the attacks the glands on both sides of the neck, in the axillæ and groins became more enlarged and tender; these subsided when the temperature settled. On 14th February 1930, the blood count showed Hb. 62 per cent., red cells 3,510,000, white cells 5,600 (polymorphonuclears 20 per cent., eosinophils 2 per cent., lymphocytes 65 per cent., hyalines 12 per cent., basophils 1 per cent.). On 24th February, during another severe pyrexial attack with a temperature up to 105°, there were again pains in the joints especially in the hips, and blood examination showed white cells 2,800 (lymphocytes 98 per cent., hyalines 2 per cent.). Shortly after this the child died in an extremely anæmic state. The irregular pyrexia during the course of the illness is illustrated by Fig. 12.

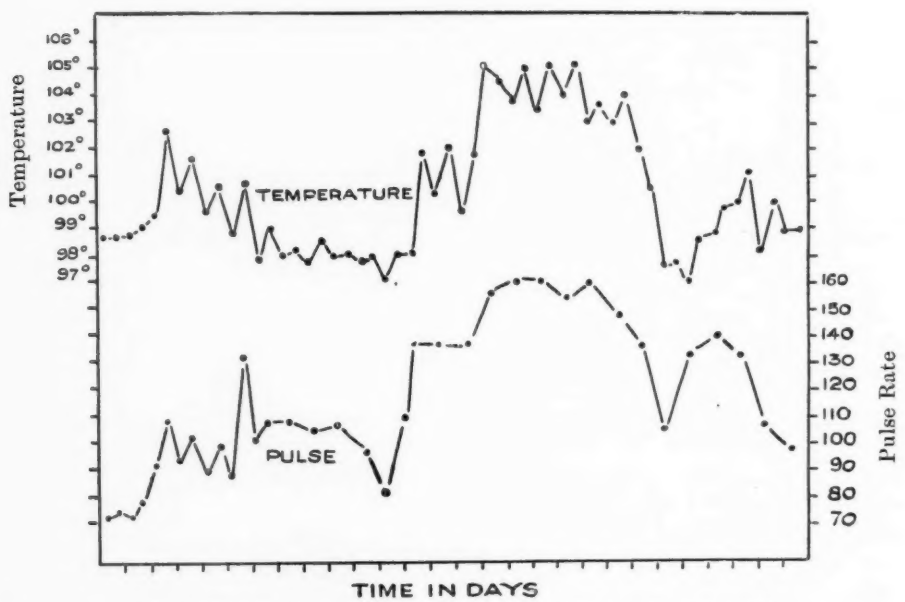

FIG. 12. Temperature and pulse rate in leukæmia (Case 22).

The tendency of hæmorrhage to occur at an early stage has already been mentioned. The slightest trauma results in bruising and bleeding from the gums, and may lead to confusion with scurvy. The tonsils are enlarged, ragged, ulcerated and bleeding. Subconjunctival and cerebral hæmorrhages are not rare and purpuric spots may be scattered all over the body. Any drug which tends to produce a rash may precipitate widespread purpura. This

abnormal tendency to bleed is associated with a low platelet count. The importance of this has been demonstrated by McLean and Caffey[9], who showed that in a series of nearly 200 cases of diseases in children the platelet count was abnormally low in six. These included the three cases of leukæmia. Apart from the clinical picture, the blood is diagnostic but needs expert examination. The value of the hæmoglobin is always low but shows considerable fluctuation. The colour index is very variable and may be as high as 1·0, or as low as 0·4. The red cells show moderate anisocytosis, poikilocytosis and polychromasia : nucleated forms are often present in considerable numbers. The white cell count may be very high indeed, and we have encountered a figure as high as 1,450,000 per c.mm. in a case of lymphocytic leukæmia. This is exceptional, but figures of 200,000 are more common. In adults the count is usually high and low counts are rare, but in children low counts are common. The differential count of the white cells is of more importance than the absolute value. High white counts are of course found in other conditions, notably in whooping cough where a count of 60,000 is not infrequent, and even higher counts have been recorded. In lymphocytic leukæmia it is the rule to find immature white cells such as lymphoblasts and pro-lymphocytes in considerable numbers. In grave secondary anæmias it has already been mentioned that immature forms such as myelocytes or lymphoblasts may be met with, values up to 5 per cent. being common, but in leukæmia the values are commonly between 10 per cent. and 20 per cent. Any case in which the percentage number of lymphocytic forms is over 70 is strongly suspicious of leukemia, and when any considerable number of immature cells is present in addition, the diagnosis may be regarded as certain. In such cases examination of blood films at intervals will usually show periods during which the lymphocytic forms reach a total of over 90 per cent.

In myelocytic leukæmia the spleen is very much enlarged and usually reaches well below the umbilicus. Perisplenitis, manifested clinically by a rub, is very common. The glands are usually enlarged, particularly in the abdomen, where they may be felt by bimanual examination with one finger in the rectum. Purpuric eruptions are common, as also is intermittent pyrexia. There is often a vague history of general ill health during the preceding one or two months, but the general course after the case comes under observation is usually very rapid. Examination of the blood shows changes in the red cells as described in lymphatic leukæmia, although there is in this case a greater proportion of nucleated forms. The white cell count, in contra-distinction to lymphocytic leukæmia, shows a high count from an early stage, the number rapidly rising to over 100,000. The differential count shows a high percentage of true myelocytes and transitional forms.

Chloroma may be regarded as a special variety of leukæmia. It is a rare form and is best illustrated by Case 23.

Case 23. S.H., æt. 6, was admitted to hospital on account of recurrent bouts of pyrexia, pains in the limbs and vomiting. He was treated with large doses of sugar, and improved markedly. Two months later the attacks recurred, and were accompanied by drowsiness and slight neck rigidity. The cerebro-spinal fluid was normal. Shortly after, he was noticed to

become anæmic, and blood examination showed: Hb. 70 per cent., red cells 5,800,000, C.I. 0·6; white cells 6,600 (polymorphonuclears 59 per cent., lymphocytes 37 per cent., eosinophils 4 per cent.). The anæmia and the drowsiness increased, and blood examination 6 weeks later gave 59 per cent. hæmoglobin, the white cell count remaining the same. At this time (6 months after admission) slight proptosis of the right eye was noticed, and this steadily progressed. Shortly afterwards the hæmoglobin value was 22 per cent., and the red cells showed considerable anisocytosis, some polychromasia, and a few nucleated forms were seen. The white cells were now 1,400 (lymphocytes 78 per cent., pro-lymphocytes and lymphoblasts 4 per cent., polymorphonuclears 18 per cent.). He was transfused with only a temporary effect. The proptosis was much more marked and a definite tumour could be felt in the temporal fossa. A week later the C.S.F. showed 0·089 per cent. protein with an increase in the globulin, and 2 cells per c.mm. The total white cells were now 19,000 with 83 per cent. lymphocytes and 8 per cent. of immature lymphocytic forms. At autopsy a week later typical deposits of chloroma were found in the right orbital fossa, extending into the temporal fossa.

Glandular fever tends to occur in epidemics and is characterized by a sudden onset of fever, with tender enlargement of the lymphatic glands, and an enlarged spleen which is often tender and rather soft. The liver is slightly enlarged but never to the extent met with in leukæmia. The temperature may be intermittent and after an acute course of two or three weeks tends to subside. Minor relapses are common, and it is often six or seven weeks before the temperature becomes normal. The blood shows moderate anæmia, the main points of interest being in the white count. There is moderate leucocytosis of 15,000 to 30,000, and in six cases which we have observed the differential count has invariably shown a rise in the number of mononuclear (hyaline) cells. Immature hyaline cells are often present in considerable numbers.

Malignant disease is a rare cause of anæmia in childhood. It includes such forms as sarcoma of the kidney, teratomata and tumours of the suprarenal glands. The cause of the anæmia is usually obvious, but a left renal sarcoma has been mistaken for an enlarged spleen, and tumours of the suprarenals with secondary deposits in the temporal fossæ may be thought to be the deposits of chloroma.

Von Jaksch's anæmia pseudo-leukæmia infantum.—In 1889, von Jaksch[19] drew attention to a form of severe anæmia occurring in infants associated with considerable enlargement of the spleen, and a blood picture showing a high white count, a relative and actual lymphocytosis and fairly numerous myelocytic cells; normoblasts and megaloblasts were also described as being present. Authorities have differed in regarding this condition either as a definite entity or as a type of infantile reaction not necessarily due to any single cause. Poynton, Thursfield and Paterson[14], for example, hold the former view, but admit that one of the cases they describe 'affords some support to the arguments of those who, unlike ourselves, believe that von Jaksch's disease is not a clinical entity, but an unusually severe stage of any infantile anæmia, the uncommon features being merely an expression of the severity of the intoxication.' Krumbhaar[18], on the other hand, states that the anæmia 'is in all probability not an independent condition, but represents an atypical response of the infantile hæmopoietic system to one or other of the primary diseases of the blood.' While not subscribing to the view that the condition is 'an unusually

severe stage of *any* infantile anæmia,' from the material at our disposal we are strongly of the opinion that the picture described by von Jaksch may be found in a number of conditions, certainly not entirely dependent on severity, for the picture may be maintained for a long time during recovery, whereas others rapidly proceeding to a fatal termination may never exhibit the characteristic features. Aschenheim and Benjamin[20] found rickets in their cases: we have encountered the association, but it is by no means invariable. Giffin[21] thinks the condition is the infantile form of splenic anæmia: in discussing the latter condition we have shown that splenic anæmia may occur in childhood without the picture described by von Jaksch. Von Jaksch himself appeared more concerned in differentiating the disease from true leukæmia, and was impressed by the number of illnesses showing a picture closely related to that of leukæmia.

The discussion is not of purely academic importance, for if the view we take is correct, the prognosis and treatment become those of the underlying conditions. This perhaps accounts for the varying statistics given by different writers as to the effects of treatment. Case 8 is that of a child suffering from acholuric jaundice which presented the features described by von Jaksch. In infancy the picture was that of von Jaksch's anæmia but later the characteristic features of this condition largely disappeared leaving the underlying condition unmasked. Had an estimation of the fragility of the red cells been made in the early stages, a diagnosis of acholuric jaundice would almost certainly have been made. We feel that most, if not all of the cases described under this heading could be classified in one of the groups described earlier in this paper.

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SPONTANEOUS NYSTAGMUS IN CONGENITAL SYPHILIS

BY

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The phenomenon of spontaneous nystagmus, of otitic origin, in children the subjects of hereditary syphilis, is one that is well known to the continental otologists. It is constantly referred to by them in their writings and lectures, but does not appear in the English literature devoted to pædiatrics, otology or syphilology.

Hennebert[1] drew attention to the syndrome, and it goes by the aponym 'Hennebert's syndrome,' or 'fistel symptom ohne fistel' (fistula symptom, without fistula). Alexander[3] and Ruttin have subsequently recorded their observations.

According to these otologists, children afflicted with hereditary syphilis may exhibit one or other of the following :—

1. Attacks of giddiness and nystagmus, coming on spontaneously, and noted by the parent. The attack is of short duration, and may be precipitated by pulling on the tragus or insertion of a finger in the external auditory meatus. It is not a constant phenomenon and is transient.

2. In this group, on a routine examination, it is discovered that by compression or aspiration of the air in the external auditory meatus, using a Siegle's speculum, or even by mere compression with the finger in the external auditory meatus, spontaneous nystagmus can be elicited. On otoscopic examination, an intact tympanic membrane will be found. Hence the description, 'fistula symptom, without fistula.' Again the phenomenon is not constant, but transient, that is to say, it cannot necessarily be elicited at any other given time. Such significance is attached to the demonstration of this sign by the continental observers that it is taken to be pathognomonic of hereditary syphilis. It is not a common phenomenon, and is not present in all cases of this malady.

Anti-luetic treatment is said to cure the condition.

Alexander[3] states, inter alia, in discussing this symptom that 'no cause is known, that it occurs from the age of 3 months onwards, that it may be continuous or periodic, that giddiness and nystagmus occur, and that pulling on the tragus or compression of the meatus with the finger will produce the phenomenon.' He also gives two aural stigmata that are characteristic of congenital syphilis, namely, a shortened bone conduction with normal hearing, and the 'fistel symptom, ohne fistel.'

Hastings[2] records a case in a girl of 20, where it was this symptom that led to the diagnosis of hereditary lues. This patient was deaf in the left ear. The membrane was intact, and compression of the meatus gave nystagmus to the right, and caused giddiness. She also had two other stigmata of the disease, interstitial keratitis and Hutchinson's teeth. Three weeks later Hastings was unable to elicit the nystagmus again.

The pathology of the condition is not settled as yet. Alexander considers it due to weakening of the annular ligament which encircles the foot piece of the stapes and anchors it in position. Ruttin is driven to the assumption that it is due to some congenital change affecting the inner ear. The varied nature of the opinions hazarded is due to the fact that congenital lues is not a lethal disease ; that the few cases that have come to autopsy with a report as to the condition of the ear, no record of spontaneous nystagmus was elicited. There is yet to be recorded the findings of the middle and inner ear in a case in which Hennebert's syndrome has been previously observed.

The phenomenon is not a common concomitant of the malady, and an explanation may be suggested more consistent with its variability, its transiency, its reaction to anti-syphilitic treatment, and its rarity. It is well known that in a case of chronic suppurative otorrhœa, a fistula symptom develops if the osseous covering of the horizontal semi-circular canal is eroded by the suppuration. If this osseous wall is destroyed by a gummatous infiltration, or is thinned by a process comparable to that which produces cranio-tabes in the vault of the skull in congenital syphilitics, the same condition obtains as in a fistula. Thus any variation in the intra-tympanic pressure is readily transmitted to the horizontal semi-circular canal, and so produces the ' fistula symptom without fistula ' syndrome. This would account for the infrequency of the phenomenon, as it is only when the thinning process is localized to the layer of bone over the horizontal semi-circular canal that the nystagmus is produced.

Through the courtesy and encouragement of Dr. D. Nabarro, I was able to examine some 40 cases of congenital syphilis, in search of any symptoms similar to those recorded above. The attached figures shew the results obtained.

In no case had the nystagmus been recorded or observed by the physicians under whose care the children were, nor had the parent in any case observed it. Only by testing the children for nystagmus was the symptom detected. All the children examined were under anti-luetic treatment for years, many from birth to 12. No occasions presented for the examination of any of the cases before treatment had been instituted.

The results of these examinations were as follows :—

Number of cases investigated ..	40.
Ages	3 months to 18 years (29 cases between 1 and 12 years).
No nystagmus elicited	27 cases.
Nystagmus	13 cases.
? other origin than ear	5 cases.
True spontaneous nystagmus ..	8 cases.

The doubtful cases were as follows :—

1 case aged 5 was a mental defect and the subject of fits ;

1 case had bilateral chronic suppurative otitis media ;

1 case was blind and the eye movements were inco-ordinate ;

2 cases had a strabismus and the nystagmus was elicited without them wearing their spectacles.

The positive fistula symptom cases were as follows : the tympanic membrane was intact in all the cases.

Case 1. Age 12, male, spontaneous nystagmus not increased by compression of the meatus. Nystagmus horizontal to one side only, transient and not consistent. Many stigmata of congenital syphilis, e.g., rhagades, Hutchinson's teeth, hoarseness, etc. W.R. negative.

Case 2. Age 12, female. Finger in the left meatus produces nystagmus to the left. It is slight and transient. W.R. positive.

Case 3. Age 10, female. Nystagmus to the right slight, with or without meatal pressure. W.R. positive.

Case 4. Age 9, male. W.R. negative. Nystagmus to the right, slight, horizontal, and unaffected by increased meatal pressure.

Case 5. Age 9, male. Horizontal nystagmus, ? slightly increased by meatal pressure. W.R. positive.

Case 6. Age 5, female. Marked nystagmus to the left, increased by meatal pressure. W.R. positive.

Case 7. Age 11, female. Nystagmus to the right, slightly increased by insertion of finger in the left meatus. W.R. positive.

Case 8. Age 10, female. Slight transient nystagmus to the left, horizontal. Not increased or affected by the compression of the meatus. Has interstitial keratitis. W.R. positive.

Summary.

1. All the cases investigated are those who have been subjected to anti-luetic treatment, many for years or from birth, so that the incidence of the spontaneous nystagmus is that amongst treated cases. No untreated cases were examined.

2. In all 8 cases the drums were intact, and as far as could be elicited the hearing was normal.

3. No vestibular or caloric tests were performed for obvious reasons.

4. The phenomenon was not a constant one.

5. Although spontaneous nystagmus was elicited in these cases, no one instance satisfied the criterion of Hennebert, namely, that compression and rarefaction of the column of air in the meatus produced an exaggeration of the nystagmus.

6. Thus one is driven to the conclusion from this small series of cases, that nystagmus, as tested for in the usual manner, is a not uncommon concomitant of hereditary lues, among treated cases in infants and children, although a true Hennebert's phenomenon was not demonstrated in any of these treated cases. What part the anti-luetic treatment has played in preventing the production of this phenomenon must remain a matter for conjecture.

The attention of pædiatric physicians is drawn to this phenomenon in the hope that all cases of hereditary lues will be examined with a view to eliciting the phenomenon. A record of their results will settle the question as to the diagnostic significance of the phenomenon in congenital syphilitics. It is the pædiatrist who sees all these cases. They do not reach the otologist, hence any early investigation must come from the pædiatrist.

I am indebted to Dr. D. Nabarro, of the Hospital for Sick Children, Great Ormond Street, for the opportunity of examining the patients at his clinic.

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THE TONSILS AND NASOPHARYNGEAL EPIDEMICS*

BY

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In a paper on nasopharyngeal epidemics presented to the Section of Epidemiology and State Medicine of the Royal Society of Medicine on 22nd June, 1928, J. A. Glover suggested an investigation into the 'relative incidence of droplet infections upon children whose tonsils have been enucleated and whose adenoids have been removed, compared with children who have not been operated on.'

I have attempted this investigation, and by reference to a small part of the literature on the subject, to discuss my observations.

The material observed is a public school for boys. A preparatory school is included, so that the ages of the boys under observation range from ten to eighteen years.

The enquiry resolved itself into two parts :—

Part 1. The condition of the throat in health.

Part 2. The incidence of catarrhal disease.

1.—A sample of the school, 289 boys in good health, was examined during the second half of July, 1929, and data relative to the tonsil, the oral pharynx, the buccal mucosa and the cervical glands noted. The figures obtained are compared with the results found in Part 2.

2,—An analysis was made of my records of the acute, non-notifiable, upper air-passage infections occurring in the same boys during the four preceding school terms. A period of approximately one year of actual observation, but including two summer terms, is therefore dealt with. Ill health during vacations is not considered.

Whereas the figures given in Part 1 may be taken as fairly typical of this class of community, those in Part 2 can in no way be looked upon as constant. They are dependent on the epidemic constitution at the time, and in the locality of the observation. Any conclusions drawn from this comparison can relate only to these particular circumstances. The setting during this period was one of epidemic sore throat, but apart from the fact that an epidemic of streptococcal tonsillitis might be expected to bias the figures against the much maligned tonsil, the writer believes his conclusions are reasonably true for all acute catarrhal upper air-passage infections.

It must be remembered that this semi-isolated community provides an environment favouring the spread of what, in the present state of our knowledge, appear to be droplet infections. As Glover says 'A school seems to be designed for epidemiological study'[1], and Sydenham advises 'To fish out the species of a continued fever choose for your field of observation some large and

* Being part of an essay on 'Nasopharyngeal Epidemics in Public Schools' awarded the Sir Charles Hastings Prize, 1930, by the British Medical Association.

populous place.' One can 'fish out' very little in the small household, and yet my impression is that, broadly speaking, I find my conclusions applicable to my general practice outside School.

PART 1.

Condition of the throat in health.

Material investigated.—The 289 boys examined represent only a part of the School. They were all in good health at the time, boys sick or recently sick being excluded so that the figures in Part 1 should be of value as a normal standard. Of these boys 60, or 20 per cent., had had no illnesses during the previous four terms; 50 have been selected as 'habituals.' The latter boys were admitted to the school infirmary at least thrice during the period under survey, and are those who lost most time as the result of catarrhal infections. The 'habituals' are not necessarily bad material. On the whole they are up to the usual standard of physical development, and I think it would have been impossible for an outside observer to pick them out as 'habituals' at the time of this examination. Naturally they show signs of disease for a while after each attack, and may become seriously debilitated after a recurrence, but at midsummer they were as healthy as the rest of the school.

The time of this examination is important. Upper air-passage infections are least frequent at the end of the summer term, and these throats were seen under optimum conditions for health. Other observers have failed to distinguish between the appearance of throats in summer and winter. It is not unusual to find as many as 80 per cent. hyperæmic throats in a batch of boys seen in the winter, and a large tonsil in the winter may be one of normal size during the summer.

The main findings are shown in the following Table 1 :—

TABLE 1.

CONDITION OF THE THROAT IN HEALTH (289 BOYS).

	All cases		Never ill		Habituals	
	No.	%	No.	%	No.	%
Total numbers	289	—	60	21	50	18
Tonsils :						
present	122	42	22	37	21	42
large	59	22	8	13	11	22
removed	167	58	38	63	29	58
Remnants :						
present	120	42	23	38	18	36
large	66	23	14	23	8	16
Pharyngeal granulations	101	35	21	35	20	40
Cervical glands :						
palpable	123	43	29	48	18	36
large	82	28	18	30	11	22
Unhealthy throats	23	8	6	10	5	10

Definition of groups.

TONSILS PRESENT.—This includes all cases not operated upon, and one or two instances where a boy was uncertain whether he had been operated upon or not. I did not find a case with a natural absence of tonsil.

TONSILS LARGE.—I hesitate to speak of 'enlarged' tonsils because the term would seem to imply a pathological process. In point of fact nine of these cases showed some pathological sign and are discussed later. It is difficult to define a standard for the measurement of enlargement. In this analysis a tonsil extending beyond the posterior pillar of the fauces is said to be large. These are certainly cases in which tonsillectomy would be performed were enlargement per se considered to be an indication for removal.

TONSILS REMOVED.—This includes all cases operated upon. No attempt has been made to distinguish between dissection, guillotine enucleation and simple cutting. The age at operation was noted but has no apparent effect upon the occurrence of remnants.

REMNANTS PRESENT.—This disregards size and includes nineteen in which the remnant amounted to nothing more than a few granulations under half a cubic centimetre in size, in all probability grown since operation.

REMNANTS LARGE.—More than one cubic centimetre of tonsil substance remaining in the throat has been assessed a large remnant. In 11 per cent. of the total cases remnants exceeded two cubic centimetres and occurred twice as frequently in 'habituals' as in the 'never ill' group. Appreciable lingual remnants were seen in 10 per cent. of all cases. These are less easily observed than faucial tissue, and the figure given is, therefore, probably insufficient. They were equally distributed between 'healthy' and 'habituals' and in 4 per cent. of all cases occurred in the complete absence of faucial tonsil.

PHARYNGEAL GRANULATIONS—as seen by direct observation through the mouth with soft palate lifted. The material examined does not include boys with obvious nasal obstruction or gross adenoids—conditions thought to require curettage and treated accordingly. The granulations observed are those on the posterior pharyngeal wall which are, I believe, sometimes the cause of the diagnosis 'granular pharyngitis.' The presence of these lymphoid nodules in the pharynx is suggestive of their presence higher up in the nasopharynx, in a position where, if enlarged, they could be called adenoids. Lateral 'granulations,' those masses of loose mucous membrane immediately behind the posterior pillars of the fauces, are not included because in the presence of large tonsils it is almost impossible to observe them, a circumstance which precludes them from statistical investigation. Large lymphoid nodules are frequently seen in this region and sometimes, when the pharyngeal constrictors and the pharyngo-palatine muscles are contracted, these masses appear to be as large as tonsils. They deserve particular attention, and may be of great importance in nasopharyngeal infections. It is across this area of mucosa that the main stream of discharge from the post-nasal space passes. I should like to repeat Lowndes Yeate's experiment with indigo carmine injections into the nasal sinuses which would, I believe, show particularly active cilia along this track. In disease they are the parts most constantly inflamed. Anatomically they

are intimately related to the tonsil and it is probable that they have an equally close physiological association, acting as the catchment areas drained by the tonsils. They are so very much under cover of the tonsil that careless observation of the throat does not reveal their presence and the text-books seldom mention them. Paton[6] in his clinical notes on influenza, makes special reference to them and looks upon their involvement as peculiar to influenza. In this he is certainly wrong, for in most common colds these folds of mucosa will be seen to be red and covered with a stream of muco-pus. In tonsillitis and in all upper air-passage infections they appear more hyperæmic than the surrounding tissues, and exudate is frequently seen on them. A peep round the posterior pillar of the fauces will frequently show an extensive area of membrane in this region in faucial or nasal diphtheria.

CERVICAL GLANDS PALPABLE.—Observations on the anterior cervical glands are recorded. The posterior triangle was not examined. Some anatomical text-books teach that the posterior groups drain the adenoids and posterior pharyngeal wall. This is probably true but rubella is the only nasopharyngitis in which I have found any constant enlargement of this group. I have always associated the deep sub-sternomastoid glands with acute pharyngeal infections, and this group is included in my observations. Glands were palpable in 43 per cent. of the cases examined, and were enlarged in 28 per cent. of the same group. This fraction is dealt with in the next paragraph.

CERVICAL GLANDS LARGE.—Again there is difficulty in defining enlargement. The 28 per cent. in this category were easily felt, and many of them were sufficiently enlarged to make one anxious to exclude chronic infection. The boys were examined at midsummer and acute infections played no obvious part in the enlargement. I am satisfied that the enlargements included in this series are within physiological limits, although in one or two cases the family doctor had instituted special treatment. In three boys glands had been incised or removed, and in two of these cases large glands have survived the operation, are freely moveable, and have been so long quiescent that anxiety is no longer felt about them.

UNHEALTHY THROATS.—Under this heading pathological appearances in the throat are tabulated. It includes the following conditions :—

Cheesy matter and exudate in the crypts	3
'Specks' (typical of the streptococcal sore throat discussed later) on tonsil or pharyngeal granulations	6
Bloodstained pus in the nasopharynx	2
Relaxed sore throat, i.e., faucitis	3
Otherwise unhealthy appearance	9

Mucus or mucopus in the nasopharynx is not included, but was very seldom seen in July.

OTHER OBSERVATIONS.—Figures were also collected with regard to the appearance of the wall of the mouth. Oedema of the buccal mucosa was seen in 6 per cent. of the cases examined and appeared to be more frequent in boys frequently ill. A boggy mucous membrane is very commonly seen in naso-

pharyngeal disease and is most obvious along the line of junction of the teeth when the jaws are closed. There is sometimes a marked ridge in this region, and desquamation occurs along the crest of this ridge. This desquamation is very similar to that seen in the region of old Koplik's spots. Minute petechiæ are also fairly common in the normal mouth but occur in the region of the back molars, a little behind the usual location for Koplik's spots. They are surprisingly constant in this position although they may occasionally be seen on the fauces and soft palate. Sometimes they desquamate and may then be confused with Koplik's spots, but they are never bluish in colour neither have they an areola. These petechiæ were seen in 9 per cent. of the boys examined and were evenly distributed among the groups discussed. They are mentioned here because it is believed that they greatly increase in incidence in the presence of certain naso-pharyngeal infections, and figures are quoted for purpose of control. Hill[12] mentions a relationship between permanent turgidity and overgrowth of the nasal and buccal mucosa and sexual development. I find no evidence of such a connection.

Discussion.

It was hoped that this investigation would permit conclusions to be drawn as to the value of tonsillectomy in the control of the common naso-pharyngeal infections. The data in Table 1 suggests that some benefit is to be obtained from removal of tonsils for, whereas the figures for tonsillectomy are the same for 'habituals' as for the mean of the School, operation has been performed a little more frequently in those cases tabulated as 'never ill.' The advantage is, however, small—but 5 per cent.—and may have been gained by the provision of adequate airway or by the removal of chronically infected tissue. It is almost negligible and not outside the limits of possible statistical error. Further discussion of this subject will be postponed until the incidence of sickness in the presence or absence of tonsils has been considered.

Of 167 operations, 60 (36 per cent.) are considered as being surgically successful; 11 cases of lingual remains and 19 cases in which the remnants were very small are included among the successful cases so that in only 30 (18 per cent.) was complete eradication performed. Paton[4] found no tonsil visible in 46 per cent. of operated cases. In no part of his paper does he mention lingual tonsil. Coues[2] found 30 per cent. of tonsillectomized children suffering from chronic tonsillar hypertrophy whereas in 12 per cent. of my operated cases the remnants amounted to normal or large tonsils in size. Although there is considerable variation in these figures, the general conclusion must be that in the majority of cases operation has failed to eradicate tonsillar tissue.

Can it be that in the 'never ill' group operation has been more complete than in the 'habitual' group? The proportion of operations considered to be successful was found to be the same in both groups; remnants, particularly large remnants, being less frequent in the sick than in the healthy, to an extent which cancels the excess of operations in the 'never ill' group.

Over 50 per cent. of 122 unoperated cases showed large tonsils. Coues[2] reports 72 per cent. with 'marked chronic tonsillar hypertrophy' but he found no case of acute tonsillitis among 212 children at the time of

examination, and he appears to have been dealing with a healthy community. But Coues' operation rate was only 20 per cent. against my 58 per cent. I take it that the majority of the operations in this 58 per cent. were performed for enlargement, and had my material been less well cared for my figures for enlargement might well have approached his. It appears, therefore, that large tonsils are the rule rather than the exception, and it is not easy to find an indication for surgical alteration of this rule on account of size only. Operation for simple enlargement continues to be a common practice in spite of considerable clinical evidence demonstrating its uselessness.

Kaiser[3] examined 5,000 cases and found that, in the absence of obstruction or obvious infection, there was no change in the patient's condition a year after operation.

Paton[4] has made a careful analysis of 424 cases, and, writing on the same subject in the reports of the St. Andrews Institute for Clinical Research[5], says 'it is difficult to believe that there is justification for so widespread an attack upon a normal structure of the body.'

Coues, however, puts a different interpretation on his results. He writes:— 'these figures show the need for keeping up and increasing this work' (of tonsillectomy).

TABLE 1A.

COMPENSATORY HYPERTROPHY OF OTHER LYMPHOID TISSUE AFTER TONSILLECTOMY.

	No operation		Operation	
	No.	%	No.	%
Total numbers	122	42	167	58
Pharyngeal granulations	35	35	66	65
Glands:				
palpable	49	40	74	60
enlarged	32	39	50	61
Unhealthy appearance	16	70	7	30

Large tonsils are much less frequent in the healthy than in the 'habituals.' At first sight this observation suggests an argument in favour of tonsillectomy, but it must be remembered that the tonsillar enlargement is post hoc and not propter hoc to disease and is probably physiological and not pathological. This remark also applies to pharyngeal granulations which are most obvious in the habitually ill and in operated cases (vide Table 1A). Paton[4] found that granular pharyngitis was present in 24·8 per cent. of unoperated cases and that this figure rose to 30·7 per cent. in operated cases with remnants and 38·1 per cent. in those in whom eradication of the tonsil was complete. He concludes 'it is evident then that the tonsil adenoid operation is followed by compensatory hypertrophy of the lymphoid tissue of the pharynx.' My figures appear to justify the addition of the words 'in the presence of acute U.A.P.I.* for these granulations can be seen to 'grow' during catarrhal infections in

* U.A.P.I.—Upper Air-Passage Infections.

the same way as remnants become apparent in the presence of acute inflammations. Moreover they were found to be scarcest—but 20 per cent.—in the clean operation cases of my ' never ill ' group. Table 1A shows some further evidence of compensatory hypertrophy in the figures for cervical glands.

Returning to Table 1, it will be seen that there is little difference in distribution between palpable and easily felt glands in the various groups. Those cases in which enlargement was sufficient to give suspicion of disease were associated as follows :—

Small tonsils..	2
Large tonsils	1
Remnants	3
Large remnants	1
Clean	1

figures too small to permit conclusion, but certainly not associating adenopathy with tonsillar enlargement in health. Glands above suspicion are slightly more numerous in boys not subject to U.A.P.I. and in boys upon whom tonsillectomy has been performed. This even distribution of glands is unexpected. It contradicts the traditional text-book teaching, and seriously challenges the statements of many writers, including Pentecost[7], who found improvement in the cervical glands and common colds in 800 children examined after tonsillectomy. Davis[8] anticipates my conclusion when he states that tonsillectomy offers no diminution in the liability to glands in the neck.

It must be remembered that the anterior cervical glands drain the mouth as well as the fauces and pharynx. Glandular enlargement is common during the eruption of the teeth and George H. Wright[9] has pointed out that enlargement of tonsil may be physiological and of a temporary character dependent on the stimulation accompanying the four periods of molar eruption. He might have mentioned the submaxillary and tonsillar glands with the tonsil.

Perhaps the greatest interest is centred round the high percentage of glands in the ' never ill ' group and reference to Table 2A will show that large glands were not found in any boy who had suffered from a complication.

Ledingham and Arkwright[10] refer to Goppert's work on meningococcal infections, which showed that glands were more frequently found in healthy contacts than in meningitic patients. Busse[11] confirms the suggestion that lymphoid hyperplasia protects from, rather than predisposes to, nasopharyngeal infections.

I believe the position is much the same in the presence of acute upper air-passage infections. Adenitis is frequently more obvious in the absence of tonsil than when the tonsils are present and acutely inflamed. I have not yet met an epidemic of glandular fever or the pseudo-glandular fever in which adenitis is a marked feature of a naso-pharyngeal infection, and I hesitate to make this statement in unequivocal terms.

Paton[5] writes : ' Tonsillar disease sufficient to induce *glandular enlargement may be present without enlargement of the tonsil* ' in relation to the examination of a number of healthy school-girls. I suggest that there is no

justification for mentioning disease, and that the statement in italics (which are mine) is sufficient in itself. The same writer[4] gives figures from 428 girls, and concludes that the 'completeness or incompleteness of the enucleation does not affect the incidence of enlarged glands.'

Pathological appearances were observed as frequently in the 'never ill' group as in 'habituals' but 70 per cent. of them occurred in boys not operated upon. This is what would be expected and, since lymphoid tissue is the only nasopharyngeal tissue demonstrating easily observed signs of inflammation, the percentages shown in Table 1A for unhealthy throats are really meaningless. In no case was the unhealthy appearance associated with ill health at the time of examination, and the history of the boys concerned was good. Four were 'habituals,' six are included in the 'never ill' group, the same number had remnants and one had no tonsils but an œdematous uvula. The morbidity amongst these boys was 74 per cent. and the average number of admissions 1·26, both figures below the average for the school. Three only gave evidence of chronic tonsillitis, and have since been operated upon, but one cannot help fearing that some of the others—particularly the 'never ills'—are immune carriers in whom a surgical spring-clean is indicated for the good of the community. And yet how difficult it is to bring home the charge against them, until our knowledge of the bacteriology of the nasopharyngeal infections has emerged from its present chaotic state, and until the importance of the immune carrier in droplet infections becomes more fully appreciated by the profession and public at large.

Conclusions.

A survey of the throat appearances of healthy school boys shows that tonsillectomy fails to eradicate tonsillar tissue in the bulk of cases. Reduction, by operation, of the amount of tonsillar material is followed by a compensatory hypertrophy of other lymphoid tissue in the neck. This hypertrophy appears to be stimulated by catarrhal infections but is least marked in boys frequently attacked by nasopharyngeal disease and those suffering from complications.

In cases still possessing tonsils hypertrophy of the tonsil is more the rule than the exception and is most frequent in boys habitually ill.

These findings suggest that there is an optimum amount of lymphoid tissue necessary for the protection of the body from nasopharyngeal diseases and their complications. Removal of part of this tissue by operation is followed by a physiological replacement in the same or other regions of the neck. Until this compensation has occurred there is increased liability to catarrhs in susceptibles.

PART 2.

The incidence of catarrhal disease in relation to throat appearances in health.

Before proceeding to discuss my figures under this heading I must emphasize the fact that my observations are limited to a period of four school terms. The epidemic state of affairs in a semi-isolated community is constantly changing and for this reason I must weary my readers with descriptions of the conditions met during the period under survey.

Recent history of nasopharyngeal infections in the school.

The period dealt with in this paper—May 1928 to July 1929—was unusually healthy. It was preceded by a Lent term in which a typical influenzoid epidemic with a steeple-like incidence curve involved 30 per cent. of the school. The zenith was reached on February 14th, when fifty-six of three hundred and thirty boys were ill. The infection appeared to have exhausted itself in five weeks but was followed by a slowly descending curve of trailers. Pneumococci predominated and an indefinite Type IV organism was found in almost pure culture in post-nasal swabs taken from nine boys in adjacent beds at the same time. The disease increased in virulence with passage and six cases of Type 1 pneumonia (one fatal) resulted about March 1st. To my mind there is very definite evidence of mutation of coccal type in vivo in pneumococcal fever. Two undoubted cases of 'influenzal' jaundice occurred. Schroder and Cooper[36] have described a similar explosive epidemic in a childrens' home—a Type V pneumococcus being causal. Streptococcal sore throat next appeared, otitis media was unusually common and three mastoids (all streptococcal), resulted, the first of them on March 19th.

The Summer term of 1928, with which the period here discussed begins, was very healthy. Febricula and coryza recurred sporadically and were associated with a few other cases of streptococcal sore throat. Some mild gastro-enteritis occurred in a short epidemic without signs in the upper air-passages. It was attributed to pollution of an open-air swimming bath in which fæcal organisms had become concentrated.

Michaelmas term opened in much the same way. Streptococcal sore throat was constantly present, and one severe acute nephritis of the hydræmic type was detected. At the beginning of December the speckled sore throats increased in severity and prevalence, and otitis media again became frequent. Lent term 1929 was peculiar. Influenzoid was sporadic only, although in other schools and in the outside community there was a marked and serious wave. Freedom of a school in the presence of an epidemic outside is by no means an unusual phenomenon, and examples of it have been observed at King's College School, Cambridge[23] and at Rugby School in November 1928[14]. This immunity was not due to any attempt at prophylactic vaccination. The weather was particularly bad with long frosts, and visiting football and hockey games were cancelled. A pneumococcus was, however, with us and a steeple-like wave of apyrexial and often symptomless catarrh spread over the school, giving rise to 'pink-eye,' which incomplete and not absolutely convincing investigation proved to be pneumococcal of low mouse virulence. Koch-Weeks bacillus was not found. The catarrh persisted for some weeks in a few cases and was most troublesome in the adults of the community. Two adults contracted pneumococcal pneumonia of low virulence at the end of the wave, and one died after a relapse due to an unidentified diphtheroid. Of these pink-eye cases twelve were pyrexial and were admitted to the infirmary. They are included in my figures as febricula and coryza. The immunity of the school from influenza may be attributed to the fact that the general epidemic outside did not commence until mid-January, soon before the school had started[19] and

very little contact with the outside world was allowed owing to the hard weather. On the other hand the conjunctivitis, as soon as it became evident that an extensive epidemic was imminent, was met by a universal dropping into the eyes of 1 per cent. mercuro-chrome, a process which was repeated three or four times. The instillation of antiseptics into the conjunctival sac in the prophylaxis and treatment of nasopharyngeal infections is no new idea, but I doubt if the school's freedom from influenza can be attributed to it, although I think the method is worth a further test. Our immunity coincided with the administrations of a vitamin B preparation to the whole school, and it appeared that while this preparation was being used the health of the school improved. I have since had cause seriously to doubt this association.

TABLE 2.

INCIDENCE OF ACUTE NASOPHARYNGEAL DISEASE.

	All cases		Habituals		Tonsils							
					No op.		Large		Op.		Remnants	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Population at risk ..	289	—	50	—	122	—	59	—	167	—	107	—
Totals :												
Boys sick	238	82	50	100	99	81	52	88	139	83	96	90
Admissions ..	441	156	174	348	188	154	98	166	253	151	166	155
Details :												
§A. Boys sick :												
Sore throat ..	171	59	41	82	85	70	46	78	86	51	61	57
Coryza and febricula	105	36	35	70	35	28	18	30	70	42	39	27
Gastro-enteritis ..	30	11	11	30	13	11	7	12	17	11	11	12
§B. Admissions :												
Sore throat ..	233	81	84	168	118	97	64	108	115	68	80	75
Coryza and febricula	149	52	67	134	52	43	26	44	97	58	53	50
Gastro-enteritis ..	33	11	15	30	14	11	7	12	19	11	13	12
Influenzoid (trailers)	14	5	6	12	4	3	1	2	10	6	8	7
P.U.O., etc. ..	13	5	2	4	—	—	—	—	13	8	5	10
Total		156		348		154		166		151		155
§C. Morbidity of Susceptibles :												
Sore throat ..	—	136	—	249	—	127	—	139	—	134	—	131
Coryza and febricula	—	142	—	191	—	148	—	144	—	138	—	140

Speckled tonsils became more frequent about the end of February, and continued in a scattered incidence throughout the rest of the term and the following summer term. It was accompanied as usual by febricula and common cold. There was evidence of the usual seasonal decline in U.A.P.I., but summer failed to give us absolute freedom, doubtless on account of the endemic streptococcal parasitism which shows no marked seasonal variation

Rubella produced a widespread epidemic during this summer term. The first few cases were isolated but the extension of the disease was not controlled. Isolation was, therefore, discontinued and the disease was treated in the school, except when symptoms were marked and malaise incapacitated boys. No other notifiable diseases occurred.

Definition of terms.—The material examined in this section is the same as that described in Part 1 and the definitions of Table 1 apply to the headings in Table 2. Certain items in the left hand column of Table 2 require extensive consideration and are dealt with later under ' discussion of diagnosis.'

The percentages in section A—' Boys Sick ' and section B—' Total Admissions ' are percentages of the population at risk shown at the head of the columns. The reader may find it easier to multiply these figures by ten when they represent morbidity per 1,000. In section C, which records morbidity of susceptibles, the divisor is the number of boys sick with either sore throat or coryza, i.e., section A. This figure represents the number of known susceptibles to either of these conditions. Thus :—

$$\left.\begin{array}{l}\text{Morbidity of sore throat}\\ \text{susceptibles with large}\\ \text{tonsils}\end{array}\right\} = \frac{\text{Admissions for sore throat of boys with large tonsils}}{\text{Boys with large tonsils sick with sore throat}}$$

$$= \frac{64 \times 100}{46} = 139 \text{ per cent.}$$

Boys sick and total admissions.—This includes all cases admitted to the infirmary for pyrexial catarrh of any type, rubella excepted. The mildest indisposition was excluded from school for observation and any temperature over 99·4 is recorded as a pyrexia. It will be clear that the total of boys sick is not the aggregate of figures for boys sick from the several conditions. A boy susceptible to both coryza and sore throat will figure as one case in the total but as two in the aggregate—one in each of the coryza and sore throat groups.

Sore throat.—This term is used here to represent a specific disease and not a symptom. The type of disease is described and discussed later and inclusion in this group depended upon the observation of characteristic exudate on the patient's throat.

Coryza and febricula—This group contains those catarrhs which could not be placed into the other groups. It is the pool into which cases of naso-pharyngeal infection showing no distinctive sign have been put and therefore contains many cases which should appear in other sections.

Gastro-enteritis.—Epidemic diarrhœa and vomiting are the criteria for inclusion in these sections. Pyrexial acidotic vomiting and feverish dyspepsia occur occasionally but are not included in this paper as I am not sure where to put them. They probably come into this group.

Influenzoid.—These cases are most probably sporadic trailers of what I prefer to call pneumococcal fever. Although the bacteriology was not investigated they were typical of the epidemic cases of Lent term 1928 and

resemble Simey's second type of febricula[14]. They differ from the febricula of my period in many ways but most definitely in that :—

1. At the onset the temperature is sub-normal and the pulse temperature ratio very high—temperature 95·6, pulse 120 is a common ratio. Within six hours this ratio is reversed and becomes low.
2. The ' grip ' is obvious and the onset particularly sudden. Unbearable malaise is, as a rule, the only symptom at onset.
3. The skin reaction is marked ; a moist, flushed skin with profuse sweating is usual.
4. Apart from slight generalized œdema of the nose, throat and mouth, anginal signs are absent.
5. Prostration is marked. These boys curl up under the bedclothes. They will neither eat nor attempt to read, talk or move. A case of febricula, even with a high temperature, is still a boy. Influenza takes away all his boyishness, and a ward full of influenza is silent and motionless.
6. Pyrexia is high, shows a fastigium, and falls by crisis. The plateau-like chart is easily distinguished from the irregular curve given in streptococcal infections.

PYREXIA OF UNKNOWN ORIGIN, ETC.—The bulk of these cases had pyrexia without signs. The upper air-passages appeared to be healthy and no cause for the fever was found elsewhere. They should in all probability be included under febricula and coryza. It is interesting to note that tonsillar tissue in the form of remnants was present in most cases but showed no signs of disease.

Discussion of diagnosis.

General epidemiological considerations.—The embryo epidemiologist fears that it may be a grave presumption on his part to attempt to discuss a subject at present sub judice in the hands of his peers, the Committee of investigation into epidemics in schools. He feels that certain fundamental points occur to the school medical officer as the result of his intensive clinical observations, which are missed in investigations based mainly on notifications and sickness returns. The main difficulty is in diagnosis and the definition of separate clinical entities. The notifiable and common infectious diseases of childhood present little difficulty. The febricula-like forme fruste of the notifiables can, as a rule, be classified in the presence of an epidemic, unless the forme fruste outnumbers the typical manifestation of the disease, as instanced in Glover's investigation into dropping cases of scarlet fever[1].

Febricula and some cases of pyrexia of uncertain origin are, I believe, mainly forme fruste of other U.A.P.I. I have seen a family of nine children with common colds in which a persistent rhinitis in one case has led to the discovery that the Klebs-Lœffler bacillus was the cause of all the catarrhs. Osler[13] writes ' It is not very unusual, during an epidemic of typhoid, scarlet fever, or measles, to see cases with some of the prodromal symptoms and slight fever, which persist for two or three days without any distinctive features. I have already spoken of these in connection with the abortive type of typhoid

fever. Possibly, as Kahler suggests, some of the cases of transient fever are due to the rheumatic poison.'

The steeple-like epidemics of influenzal type are easily recognized when once established, but the first cases and the trailers to the epidemics are identified with less certainty. The same must be admitted of the many different forms of tonsillitis and sore throat. Coryza is most typical in the absence of pyrexia : then it appears to be a well defined and distinct disease. But when the cold is a feverish one its differentiation from the other catarrhs becomes so difficult that Simey[14] writes ' It seems highly probable that coryza, febricula and influenza are an inseparable group of diseases beginning in the upper respiratory tract.'

The question ' Are these sub-divisions separate clinical entities ?' must be answered. Paton[5] in an admirable discussion of a series of cases conventionally diagnosed

1. Febricula or P.U.O.,
2. Vomiting or gastro-intestinal catarrh,
3. Sore throat or pharyngitis,
4. Follicular tonsillitis,
5. Bronchial catarrh,

shows how much alike are these conditions, and using as an analogy the signs and complications of measles and scarlet fever concludes ' The facts suggest strongly that some common factor underlay all the cases whose variations were determined by the activity of secondary complicating organisms. Symptoms common to all cases in all groups suggest that the common factor may have been B. pneumosintes[15] and that the epidemic was influenzal in character.' Sir William Hamer[16] would, I feel, have us think the same without mentioning B. pneumosintes.

This single pathology is a suggestion worthy of most careful consideration. It is a very attractive solution to the acute U.A.P.I. problem, but as a working hypothesis in clinical school medicine it is, in my opinion, dangerous. Only by attempting to split the atom shall we prove it whole, and I would suggest for practical purposes the opposite hypothesis, namely, that the local and general reactions to simple parasitic invasion of the upper air-passages are similar, no matter what the cause. There are, however, fine differences both epidemiologically and clinically enabling recognition of separate fevers referable to specific causes, microbic or otherwise.

Pyrexia, coryza, urgent lymphoid hyperplasia and œdema of mucous membranes are common factors. Varying types of exudate, visible coccal colonies, false membrane, local hæmolysis and hæmorrhagic oozing, typical pyrexias, vasomotor disturbances, rashes, herpes and complications may be pathognomonic of specific infections having separate identities and showing definite epidemiological characters.

Clinical observations on these lines, coupled with careful bacteriological investigations, should offer a more satisfactory solution. The subject will become complicated but when we have grown a good beard let us apply William

of Occam's razor ' Entia non sunt multiplicanda præter necessitatem,' if we dislike the growth, and can hope to find the fair face of truth underneath it.

I have remarked that an attempt to associate all acute upper air-passage infections under one pathology is dangerous. There appears to be such definite evidence that many different infections are at play, and although these may be due to secondary invasion as postulated by Paton, I am inclined to believe that such is not the case. One frequently finds two distinct catarrhs summated in the same patient, or one patient suffering from two apparently distinct diseases within a few days. This super-imposed infection may be the explanation of Paton's cases already referred to[5], in which gastro-enteritis was followed by tonsillitis and influenza by septic sore throat.

Bloomfield and Felty[17] report a carefully observed case (No. 31) in which influenza commenced on January 27th and was complicated by the onset of ' Beta ' streptococcal tonsillitis on February 1st, at a time when it is probable that both conditions were epidemic and almost certain that the attack of tonsillitis could not be the result of an auto-infection. It thus becomes clear that these conditions must be nursed separately if cross infection amongst warded boys is to be avoided.

Clement Dukes[18] remarks ' When asked, as I frequently have been, what is the matter with the throat, I am only able to plead ignorance, but I strive to impress the fact on my inquisitors that when I am able to diagnose the case at first sight I have secured it far too late for the welfare of the individual and for the protection of the other members of the school. Moreover . . . an early exact diagnosis is not necessary so long as the sufferer is transferred to a quarantine ward immediately.' Since the influenza pandemic of 1918 matters have changed. In Dukes' time influenza attacked only 8 per cent. per annum of the school in an average of the years 1871–1904, reaching its zenith in 1893 with about 25 per cent. per annum. Sir George Newman quotes[19] for a public school the following attack rate of influenza :—

1919	Lent	.. ..	32 per cent.	Per term only.
1920	,,	.. ..	46 ,,	
1925	,,	.. ..	59 ,,	
1926	,,	.. ..	12 ,,	
1927	,,	.. ..	19 ,,	
1928	Summer	.. ..	18 ,,	

This experience of influenza is by no means unusual and these figures are not high.

I believe there has been a corresponding increase in the non-influenzoid catarrhs since the war. Such infections are apparently less frequent during influenza epidemics or else are summated by influenza. Simey[14] demonstrates with figures from Rugby School the same fact, and Glover[1] produces conclusive graphs. It is this increase which makes it no longer possible to observe individual cases of catarrhs in quarantine rooms and early clinical diagnostic signs must be looked for in order that cross infection in sick wards shall be avoided. Furthermore Dukes' most formidable enemies were the notifiable diseases. The present generation of school medical officers are equally, if not

more, anxious to control the serious complications of the more indefinite acute upper air-passage infections :

Pneumonia, etc.
Sinusitis.
Otitis media, mastoid, etc.
Peritonitis.
Carditis.

Lowered exercise tolerance, depression and mental inertia ; and almost certainly acute rheumatism and acute nephritis[20].

Roseneau's dictum[21] ' Man is the source and fountain head of these infections, each case is a focus for their spread. Isolation and disinfection of the discharges are the first indications ' was said of the common cold and must be applied. Isolation is, however, not the whole solution to the problem. Dudley[22] writes ' It should be clear that isolation has failed to control the spread of infectious diseases, because it is impossible to control all the infected hosts,' and has shown that one of the many things which will reduce the carrier menace is the proper spacing of beds in dormitories and careful ventilation.

At this point it is well to remember that epidemiological curves of influenza show a high incidence of trailers after the main epidemic. We are at present on the swing back of a pandemic wave, and the possibility of the shock attack of influenza lowering the resistance of the host to secondary invaders may account for the present increase in catarrhal disease. It is improbable that the secondary invaders give any increased immunity against a second shock attack, but they may immunize against themselves.

Bloomfield and Felty[17] report a wide dissemination of other common inhabitants of the throat after influenza. In the case of the epidemic observed by them they conclude that since there was no alteration in the streptococcal parasitism they were studying that other hæmolytic streptococci disseminated were saprophytes. This is doubtful. It may be that these organisms are only apparently saprophytic and fail to attain an epidemic potential for some time after dissemination. When an effective potential matures, the standard organisms are overgrown and a new epidemic flora appears. Such was Glover's[1] experience when investigating sore throat attributed to Dochez's hæmolytic streptococcus. The original streptococcus was lost but sore throats continued with another flora. I suggest that some change in the clinical signs in the throat may have marked the disappearance of Dochez's organism, and that observation of these signs may have prevented relapses, the new disease being isolated from the old.

Streptococcal sore throat.

The standard fever of the school during the period dealt with in this paper was a ' viridans ' sore throat producing characteristic signs in the nasopharynx. Diagnosis depended on the observation of exudate, translucent and pearly in appearance, in the throat. The exudate resembled a colony on a culture plate and varied in size from a pin head to a split pea. It was generally disc-like and circular in shape. It was most easily observed on the tonsil, but both in the presence and absence of tonsillar tissue it appeared on the post-pharyngeal

granulations and was occasionally seen upon the mucosa of the fauces or soft palate. The little specks of exudate occurred on the mounds of tissue between the crypts rather than over the crypt mouths, and in the pharynx they sat like small caps on the top of the lymphoid nodules. In this respect and also in shape and colour the exudate differed from that observed in lacunar tonsillitis. The smaller specks are likely to be confused with the tiny scars occasionally seen on the surface of the tonsil. These scars are seldom circular and are of a yellowish colour. They cannot be wiped off with a swab. In a few cases the growth gave place to a definite follicular tonsillitis ; yellowish cheesy matter appearing in the tonsillar crypts. I formed the opinion that the exudation of débris from the crypts was mechanical and secondary to œdema of the tonsil produced by infection with the surface organism. One was reminded of the picture produced when a volsellum is applied to a large tonsil before dissection.

The pyrexial reaction lasted from three to five days and was irregular, with a variation of about two degrees between morning and evening readings. Growth seldom appeared until the second day and was marked on the third. Sore throat was not a marked feature unless the fauces were involved. I think it was a more common symptom in boys whose tonsils had been removed. Pain in the throat was commonly absent, headache being the main symptom. Swabs were taken from many cases and sent by post for examination. They helped to exclude diphtheria but were otherwise of little value. Streptococcus viridans predominated and was associated with hæmolytic and non-hæmolytic streptococci of two or three strains in each culture. M. catarrhalis appeared occasionally but the absence of pneumococci was conspicuous. It is obvious to the writer that the bacteriology of these conditions must be worked out at the bedside. Exudate should be ' picked off ' from the throat and planted direct on to the medium with a platinum loop. The swab is not an instrument of precision and long postal journeys are not good for microbes.

In this connection I should like to emphasize the difference between surface and tonsil-puncture cultures which has been demonstrated by other workers[29, 30] and to suggest that bacteriologists investigating the tonsils arrange for the collection of material with more care than that offered by a swab jabbed deep into a tonsillar crypt.

The specific condition described appeared to be endemic during the period dealt with in this paper, but it is not always present in the school. It was probably carrier borne, and the case incidence was similar to that charted by Bloomfield and Felty[17] showing no marked seasonal preponderance. I do not suggest that the causal organism in these cases was the beta-hæmolytic streptococcus of these writers for I have, I believe, observed two other distinct clinical forms of streptococcal sore throat. One is best described as a ' glairy tonsillitis ' in which the tissues look as though they had been smeared with white vaseline. In the other the growth is not disc-like but conforms to that lacunar tonsillitis described by Fraenkel[26].

Bloomfield and Felty[17] state : ' It was shown that either tonsillectomy or carriage of beta-hæmolytic streptococcus protected against infection ' but in a later paper[27] they admit the development of acute streptococcal infection

of lymphoid tissue of the throat, equivalent to tonsillitis in people whose tonsils have been removed.

There are probably many strains of epidemic tonsillitis apart from milk-borne outbreaks. Haig-Brown[28] watched his cases at Charterhouse with great care and describes the exudate observed as varying from 'little green dots studding the tonsil surface' and sometimes extending to a greenish or yellowish green mass spreading on the fauces. His cases appeared to occur in more definite epidemics of a shorter wave length, although they had no obvious seasonal relationship. Haig-Brown reports, out of 345 sore throats, eight cases of endocarditis with chronic valvular disease. Three boys had pericarditis and ten mitral regurgitation of a transient character. His acute rheumatism rate was proportionately high.

Drs. Griffith and Scott[1] found Dochez hæmolytic streptococcus present in an epidemic of sore throats in a school during one term, and Dr. Glover tells me that this organism produced a plum coloured tonsil without exudate. As already mentioned, in the following term the sore throats continued but Dochez disappeared. It appears to be amply demonstrated that many strains of streptococcus can produce sore throat, that of scarlet fever amongst them : that in any one epidemic one strain will predominate and may give rise to a distinctive clinical appearance in the majority of persons affected.

I have mentioned cryptic or follicular tonsillitis and suggested that it is produced mechanically in acute surface infections, given tonsils with deep crypts which will naturally retain débris. In other words there is a type of follicular tonsillitis which will only occur in tonsils from which débris can be expressed in health. The débris appears to mean little more than wax in an ear or smegma behind a prepuce and the appearance of beads of pus-like débris in the crypts during an attack of sore throat does not mean a more severe illness, and the surface organisms are more likely to be causal than those found in the débris. These latter are probably saprophytes in the healthy subject and play no part in epidemic sore throat. Simey[14] writing on febricula, says 'In some epidemics cases of true follicular tonsillitis occur but this is not the rule.' Follicular tonsillitis of this type must be distinguished from the definitely infectious 'lacunar' tonsillitis so ably described by Prof. Fraenkel[26] in which a white exudate appears over the entrance to the crypts and usually conforms to the shape of the crypt mouth. This mechanical cause of follicular tonsillitis is most probably the explanation of the occurrence of 'traumatic angina' after cautery of the nose or other intra-nasal manipulations which produce a diffuse œdema of the upper air-passages in the same way as the common cold.

Coryza, febricula.—An attempt will be made in another section to prove the contention already put forward that coryza and febricula are 'formes frustes' of the stationary fevers of a community. It appears that this conception is generally accepted. Wells[31] says : 'The consensus of the best opinions is that there is no specific cause of this troublesome infection.' I would rather say with Osler[13] 'There are a variety of causes'—a probable reason for the relapses which are so frequently observed and in which subsequent attacks may differ from each other ætiologically and bacteriologically.

I suggest that the chief ætiological factor in the cases met during the period under survey in this paper was the streptococcus, producing at the same time sore throat. To a less extent the cases of gastro-enteritis, pink-eye, pneumococcal fever, etc., brought in their train further cases of coryza and febricula, produced by their respective causal organisms. This group of coryza and febricula is therefore a polygenic collection of cases of nasopharyngitis of unknown origin in which a diagnosis on physical signs has been impossible.

Gastro-enteritis.—The thirty cases observed occurred in short bouts and appear to deserve recognition as a separate entity. The largest wave produced sixteen pyrexial attacks. They were undoubtedly nasopharyngeal infections and were occasionally associated with definite symptoms of coryza. In all cases there was an acutely unhealthy appearance of the throat, but the presence or absence of tonsils had no influence on the case incidence. Pyrexia occurred in only a small proportion of the total morbidity and these figures represent not more than a third of the total cases of 'tank trouble' as it is called in the school. These trivial epidemics are steeple-like in form and in this the common name of 'gastric influenza' is fitting. Food poisoning, polluted water from drinking and bathing, and infected milk are possible causes. Food poisoning would not have given cases over a period of a fortnight. There is a common supply of water and milk to the school and to people resident outside the school who are also under my care, and who did not suffer from the disease. The most probable source of the trouble is a droplet infection, and a slight but definite increase in febricula and coryza at the time of the gastro-intestinal epidemic supports this suggestion.

A point of great interest is the occurrence of two cases of appendicitis (one confirmed at operation) on the two days immediately preceding a wave of diarrhœa and vomiting. The total number of tender appendices in the four terms recorded was five. Recently there has been much correspondence on the association of appendicitis and sore throat or tonsillitis, and the literature makes frequent mention of measles complicated by appendicitis. Those who work in small hospitals serving, say, a market town or group of villages with fairly fixed population, may confirm my observations that appendicitis tends to occur in batches. I draw no conclusions from these notes, but suggest that the possible association between the acute appendix and acute U.A.P.I. is worth further investigation. Bowen[32] elaborates this suggestion. Poynton's[37] classical experiments with the diplococcus rheumaticus should be remembered and Cope[38] has recently emphasized the importance of blood stream infection from nasopharyngeal foci in the ætiology of the acute abdomen, although he omits to mention the common origin of these foci, the droplet infection.

'Influenzoid'—pneumococcal fever.—Simey[4] believes influenza to be inseparable from the febriculæ. To my mind it is difficult to associate the two at all closely. The distinctive clinical appearance and remarkable constancy of the epidemic curve appear to identify it without doubt from the ever present common cold group. Of course there are abortive forms indistinguishable from febricula and inseparable in this sense. It is also probable

that the mode of transmission of influenza is unlike that easily demonstrated droplet route of the stationary endemic fevers and associated coryzas. Hill[12] cites M. J. Roseneau's observation that it was found impossible to transmit 'flu from a bedridden case to another subject by a face to face talk, whereas 'sore throat' can be transmitted in this way.'

I do not suggest that influenza in all its forms is the result of invasion by one organism only. It is the influence of a particular type of epidemic invasion, each mass attack having an individuality depending upon a specific parasitism. The parasitism may vary with succeeding waves, and the many organisms described as causal may easily have been causal in the place and at the time of observation. The cases collected in this series were most probably pneumococcal fever.

Results obtained.—82 per cent. of the boys investigated suffered from nasopharyngeal disease and averaged 1·85 admissions to the infirmary per boy, the morbidity of the whole 289 examined being 1·56 per boy, (see Table 2).

These figures at first sight would appear to be high, but upon investigation they are not out of proportion with the findings of other schools, neither are they much more grave than in the general population. Slight fever and malaise is seldom reported to the general practitioner, and in some households we do not look upon a feverish cold or two per child per annum as excessive. It cannot, however, be denied that schools are, for many reasons, good incubators, and in the school under discussion about 400 people live in one building, sometimes at dangerously close quarters.

Consideration of the actual numbers in Table 2 produces little of interest. Sore throat was the predominant disease and, if my diagnostic methods are reasonably safe, one attack failed to produce more than a transitory immunity. It has been suggested that this sore throat was, for the most part, of a specific type and that the coryza and febricula associated with it was produced by the same micro-organism. If this is true, diagnosis of this particular type of viridans fever has been possible in about two-thirds of the cases involved.

The percentages are more instructive, and when the totals are considered one is impressed by an unexpected uniformity in the distribution of disease in the various columns, the differences being so small that one doubts their significance and hesitates to draw conclusions from them. Thus, with a mean susceptibility of 82 per cent., operated cases are most susceptible (83 per cent.) and of them boys with remnants stand the greatest chance of being ill (90 per cent.). Next to them boys with large tonsils show the highest attack rate (88 per cent.). There is, therefore, a definite association between morbidity and an increased amount of lymphoid tissue. A more searching analysis than is possible here has shown that the 18 per cent. of operated cases in which complete eradication of lymphoid tissue has been accomplished is the healthiest in the school. This is not because successful operations have been performed on them, but because they are healthy. A few bouts of nasopharyngitis would have caused lymphoid tissue to appear, and they would have swollen the most susceptible group, those with remnants. The greatest morbidity is, however,

in the large tonsil group (1·66 per boy) and is 6 per cent. above the mean of the school. In other words, while boys with remnants are least immune to catarrhal attack, recurrence of attack is most common in those with large tonsils —an observation possibly associated with autogenous infection and discussed later.

So far only the aggregates of all diseases have been considered. When we come to the detailed figures we find that in both sections A and B sore throat is most common in the presence of large tonsils and least common in operated cases with little or no remnants. The reverse is true of coryza and febricula, which occurs most frequently in the absence of tonsil. The less the lymphoid tissue the more uncertain the diagnosis.

Gastro-enteritis is evenly distributed in the different tonsil columns but almost half the cases—15 of 33—occurred in 'habituals.' This either brings to light a source of statistical error and shows this group to be inflated, or suggests that habitually catarrhal children are more susceptible to gastro-enteritis. I believe the former explanation to be the true one.

Influenzoid.—My figures under this section are small and hardly worthy of consideration, particularly as it is almost certain that typical influenza will appear again in epidemic form when data can more easily be collected. It is, however, obvious that what figures I have produced exonerate the large tonsil from blame, and show the incidence of influenza to be highest in the operated cases.

Discussion.

I am conscious of the limits of my investigation. My findings are true of a community of about 350 young males, observed for the comparatively short period of sixteen months and living in an environment in which risks of infection are great but types of infection few, so few that the bulk of sickness during the period was produced by one type of organism. Under these circumstances I hesitate to apply the following conclusions to all epidemics of sore throat. Some strains may have a predilection for the tonsil so that tonsillectomy may protect against infection, but in the type of infection dealt with in this paper there is little evidence to show that tonsillectomy either protects or has any obvious effect on the incidence of acute anginal conditions.

The ætiology of the common cold.—It has been stated that the pathognomonic sign of sore throat was the detection of specks of exudate. Exudate occurs on lymphoid tissue but may rarely be seen on mucous membrane. It follows that where there is no lymphoid tissue exudate is unlikely to be detected. Hence many cases which should be included as sore throat are scheduled as feverish colds. This shift is obvious in sections A and B of Table 2, and there is no real suggestion that tonsil-free cases are twice as susceptible to febricula as those with some tonsil. The coryza group has also received undiagnosed cases of gastro-enteritis, influenzoid, and probably some rubella. An estimate of the extent of this shift can be made.

I have postulated that tonsillectomy has no appreciable effect on the incidence of U.A.P.I., provided compensatory hypertrophy has occurred to replace the lost lymphoid tissue, and have shown that the catarrhs are dis-

tributed evenly irrespective of the state of the tonsil. In the epidemic condition discussed diagnosis of typical sore throat has been proportionate to the amount of lymphoid tissue present. The ratios of sore throats to coryzas are as follows :

Operation	1·17	Mean of all cases 1·56.
Remnants present	1·50	
No operation	2·26	
Large tonsils	2·46	

If these premises are true and the ratios of sore throat to coryza are corrected to 2·5 in all groups, there is but a small residue of febricula left. Similar corrections for coryzas related to gastro-enteritis, pyrexial pink-eye, rubella and influenzoid fevers will dissolve the residue for pyrexial coryza as a separate entity. William of Occam's razor will have been applied to part of the growth, and a single pathology for the endemic-epidemic febriculæ of the community under consideration established, relating them to the epidemic flora present at the time.

I have said in my general epidemiological consideration that the single pathology hypothesis is a dangerous one until proved. I repeat this warning for I have not attempted to extend this discussion beyond the limits of my own small investigation. With change of time or place other micro-organisms or other circumstances may produce similar results, and I merely contend that febricula and coryza are 'formes frustes' of the stationary fevers of a community.

Such is my tentative conclusion arrived at by a process of speculation upon insufficient figures. I think, however, the method is worth further test and I commend it to other investigators.

The influence of the chronic tonsil on the incidence of acute naso-pharyngitis and tonsillitis.—It has been pointed out that the morbidity of boys with large tonsils was 6 per cent. above the mean for the school. It is possible that part of this excess is due to recurrent auto-infection in boys with chronic tonsillitis. The presence of such cases is also suggested by the relatively higher percentage of large tonsils amongst ' habituals ' compared with healthy boys (Table 1). Three such cases are mentioned in the discussion on ' Unhealthy appearances in the throat in health ' (Part 1), but they total no more than 1 per cent. of the school. Given chronic septic tonsils and adenoids, particularly if there is nasal obstruction, tonsillectomy is definitely indicated and certainly improves the children operated upon. In this I agree with the generally accepted opinion and the conclusions of Pentecost[7] and Sington[24], but tonsillectomy does not reduce the risk of heterogenous and epidemic infection, an assertion in keeping with the findings of Kaiser[3] already mentioned.

I have found no evidence that the boy with chronic infected tonsils acts as a carrier, but a school medical officer in reply to a questionnaire circulated by the Association of School Medical Officers[25] writes ' In three years treatment of adenoids, rhinitis and septic tonsils in boys acting as sources of infection has reduced the incidence of colds.'

The school under consideration is surprisingly free from the chronic tonsil, but I take it that probably the most potent source of chronic infection is the

acute catarrh, and under these circumstances the chronic tonsil is a potential carrier. Even so, the total of such cases must be a very small part of the carrier rate required to produce an epidemic, and in my mind the chronic tonsil, although it requires attention, plays but a minor role in the spread of infection.

I have stated that not more than one per cent. of the boys investigated require tonsil operation, and I feel that a great number have already been unnecessarily deprived of some useful lymphoid tissue. I am, of course, unable to estimate the number of those cases operated upon in which operation was essential. Perhaps in no other subject is there such a great difference in the personal judgement of the surgeon and in the criteria of operability. It is possible that a further one per cent. will acquire chronic tonsillar infection during their school lives. The best way to avoid this is to protect them from droplet infections.

TABLE 2A.

CONDITIONS OF THROAT IN HEALTH OF BOYS SUFFERING FROM COMPLICATIONS TO A PRIMARY NASOPHARYNGITIS.

	All complications		Otitis media		Mean of school	Relative deficiency of total lymphoid tissue in complicated cases	
	No.	%	No.	%	%		
Total numbers	31	11	20	7	—	Less	More
Habituals	8	26	3	15	18		
Tonsils :							
Present	11	35	7	35	43	— 8	
Large	4	13	1	5	22	— 9	
Removed	20	65	13	65	58	— 7	
Remnants :							
Present	14	45	9	45	42		+ 3
Large	12	39	5	25	23		+16
Pharyngeal granulations	10	32	7	35	35	— 3	
Cervical glands :							
Present	9	29	8	40	43	—14	
Large	0	0	0	0	28	—28	
					Total	—69	+19

Complications.—Fortunately complications to the catarrhs discussed in this paper were, with the exception of otitis media, infrequent so that the figures presented in Table 2A may be too small to be significant. They are, however, suggestive and will therefore be discussed.

Although many cases of otitis media were mild and showed nothing more than earache and a flushed drum head, the other complications are those in which appreciable disease was present causing some anxiety as to ultimate prognosis. They occurred as follows :—

Acute otitis media (including three cases with grave toxæmia	20
Bronchitis, large tube	4
Bronchitis, small tube	1
Congestion with phantom consolidation	3
Congestion with pleurisy	1
Established lobar pneumonia	1
Acute rheumatism	1

I have said that in conditions other than otitis media only severe complications are included in my figures. Infection of the paranasal sinuses is, of course, very common in association with all nasopharyngeal disease, and a serous sinusitis is probably present in a large number of the catarrhs seen. Diagnosis is, however, uncertain except in well developed cases, and without special apparatus diagnosis sufficiently exact to allow statistical investigation is unattainable.

A few râles or rhonchi in the chest of a coughing boy are not included as appreciable complications, but they were seldom met during the period discussed in this paper, the predominating infection having a much greater affinity for the ears than for the chest.

Discussion.

The results obtained show that complications occur most frequently in operated cases, particularly in those in whom complete or almost complete eradication has been performed. Serious disease is infrequent in the presence of large tonsils. Habituals, who number but one-sixth of the boys examined, score one-quarter of the complications, and although, as previously pointed out, the morbidity figures in the ' habitual ' column are inflated, I am satisfied that the ' habitual ' stands in greater danger of contracting a complication merely because he is more frequently involved in a catarrhal fever.

The most interesting observation to be made from Table 2A is the marked deficiency of total lymphoid tissue. This deficiency is represented in the right hand column of the table, the figures in which are merely relative and have no statistical value. Large tonsils and palpable cervical glands are below the mean, clean operation cases produce the greatest proportion of serious disease and large cervical glands are entirely absent. On these grounds it is difficult to avoid the conclusion made in Part 1 of this paper that there is an optimum amount of lymphoid tissue in the throat and neck, the artificial reduction of which exposes the person to increased dangers.

Only two of the complicated cases had an unhealthy throat appearance in health and I feel that the chronic tonsil had little to do with the incidence of serious disease in the school. The figures produced from the twenty cases of acute otitis media examined hardly confirm Paton's[4] observation that the tonsil-adenoid operation results in an increased incidence of otorrhœa, for it will be seen that tonsils had been removed in about the same proportion as in the group ' never ill.' There is, however, ample evidence that tonsillectomy has not protected against otitis media. Fowler[33] does not give comparative figures, but 53 per cent. of his cases of otitis media had had tonsillectomy

performed, and Wright[39] surveying the experience of sixteen years, shows marked increase of this disease in spite of the increased practice of tonsillectomy. On the other hand his figures show some improvement with regard to chronic ear-disease as the result of operation.

Otitis media is the complication of the common nasopharyngeal infections which appears best to demonstrate the mixed origin of these infections. Separate waves of otitis occur, each wave appearing to have definite differences from the preceding wave: One wave, frequently when a pneumococcus is about, will produce fulminating mastoids; another probably associated with a staphylococcus aureus throat infection will show more signs of otitis externa than of otitis media, the drum-head and meatus being constantly obscured by a white membrane. In a third, pain will be intense and spontaneous perforation occur before paracentesis can be performed. In a fourth, the otitis will be of a low grade and insidious in onset, but will give a high percentage of chronic mastoids. Streptococcus mucosus will be producing common colds at this time. E. Watson-Williams[34] notes how some cases of mastoid disease without otorrhœa tended to occur in groups, and the almost constant appearance of a vesicular eruption on a dusky drumhead during the last influenzal epidemic will be remembered by many. The otitis of scarlet fever is produced by the scarlet streptococci and not by secondary invaders.

I have little doubt that these phenomena are the cause of such conflicting reports on investigations of the bacteriology of otitis media[35], and I look upon them as being strong evidence against the relation of all coryza, febricula and influenza to a single causal organism.

The importance of simple nasopharyngeal infections in the ætiology of the majority of serious acute illness is not always appreciated. Only in the case of acute rheumatism will the direct association between the appreciable diseases mentioned above and the simple acute U.A.P.I. be challenged, and a discussion of the ætiology of acute rheumatism is out of place here. It may, however, be opportune to suggest that there is evidence that some cases of many apparently unrelated and so called idiopathic conditions, for example :— essential hæmaturia, cystitis and pyelitis, cholecystitis and catarrhal jaundice, gastric and duodenal ulcer; and even some dermatoses, namely, pityriasis rosea, certain urticarias, and other allergic manifestations may originate in acute U.A.P.I. in the same way as erythema nodosum shows relation to an epidemic sore throat.

These sweeping assertions are, of course, put forward in the most tentative sense, but since observations on the common cold must necessarily be made by the general practitioner and satisfactory material will seldom present itself to the expert investigator, I feel it is for a general practitioner to redirect attention to the possibility of such an association.

Conclusions.

A comparison between the incidence of disease in, and the normal throat appearances of, healthy school boys answers the question asked by Glover[1], and taken as the text of reference for this enquiry. The figures produced admit of one certain conclusion :—

In the mass the tonsil has no obvious effect upon the incidence of acute anginal conditions, and uncomplicated nasopharyngitis occurs irrespective of the presence or absence of tonsil.

Cases of chronic tonsillitis subject to recurrent auto-infection are rare and their number is insufficient to alter this conclusion, the bulk of disease being due to transitory surface infection. The quality of lymphoid tissue is at present beyond investigation. There is, however, considerable evidence that an optimum quantity exists in the healthy throat and that this optimum quantity is greatest in the presence of nasopharyngeal infection. Reduction of this quantity by operation increases the patient's risks to invasion by an infecting organism, not only so far as simple catarrh is concerned but to a greater extent with regard to complications.

My figures give strong support to Paton's[4] conclusion that 'it is evident that those subjected to the operation were not only no better than the rest, but were actually worse in practically every particular with the exception of enlarged cervical glands.' Palpable cervical glands, even when enlarged, are seldom pathological but are most frequently physiological, and Paton could justly erase this one blot from the tonsil's escutcheon. Such physiological enlargement results from the presence of infection in the nasopharynx which also stimulates increased growth of the nasopharyngeal lymphoid tissue, the tonsil or the tonsillar remnant. The increased risk to invasion after operation is in some way mitigated by this compensatory hypertrophy of the remaining lymphoid tissue, and the absence of such hypertrophy appears to conduce to complications. The distinction between infection and invasion should be noted. When a pathological flora attacks a closed community almost every member becomes infected and the carrier rate is said to be very high. Comparatively few of the infected hosts respond with a local and general reaction sufficiently violent to constitute disease. These latter are said to be invaded. It has also been suggested that the common cold is the expression of an abortive reaction to infection, no matter what the infecting organism. The continued search for a specific cause of the common cold is not likely to establish a single pathology for this condition.

That most extensive and ubiquitous group of diseases, the droplet infections, has little to do with the tonsil or its removal. Except in the relatively rare instance where auto-infection from a chronic focus produces recurrent inflammation, acute tonsillitis is a symptom and not a disease. Tonsillectomy is symptomatic treatment in its most elementary form and its extensive application has produced no obvious beneficial result in the control of acute nasopharyngeal infections. It is a red herring which must be removed from the deep waters covering the secrets of the prophylaxis and treatment of the common cold and its many malicious relatives.

Summary.

1. An attempt has been made to assess the value of the tonsil-adenoid operation in the prevention of epidemic nasopharyngeal infections. The operation was found to be of no appreciable value, but some evidence is produced to show that it is followed by compensatory

hypertrophy of other lymphoid tissue in the presence of acute upper air-passage disease. The findings suggest that, until the loss of lymphoid tissue is made good, the operated cases are more susceptible to the common catarrhs and more frequently attacked by complications.

2. Chronic tonsillitis is a complication of acute nasopharyngitis. Autogenous reinfection from septic tonsils is not common. It is discussed and the necessity for operation in these circumstances emphasized.
3. A distinctive type of epidemic sore throat is described.
4. A tentative statistical proof that coryza and febricula are " formes frustes " of the stationary fevers of a community is presented.

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MENINGEAL HÆMORRHAGE IN THE NEW-BORN

BY

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Intra-cranial hæmorrhage is an extremely common cause of neo-natal death ; indeed, a large proportion of infants who die from the effects of asphyxia show some form of meningeal hæmorrhage. In these cases capillary oozing from the meninges is almost invariably found. Gross hæmorrhage from the meninges is also an important cause. Holland and Lane-Claypon[1] found that 25 per cent. of still births and neo-natal deaths were due to intra-cranial hæmorrhage, while Cruickshank[2], in 800 consecutive post-mortem examinations on infants who had died within two weeks of birth, found gross intra-cranial hæmorrhage in 161 cases (20·1 per cent.). Tentorial tears, often involving the straight sinus or the vein of Galen, are the most common lesions found, but hæmorrhage may arise from injury to the falx cerebri or to vessels running into the longitudinal sinus, and there may be oozing from the choroid plexus into the ventricles. Hæmorrhage into the brain itself is probably rare, but Schwartz[3] holds that petechial hæmorrhages into the brain substance, especially in premature infants, are of common occurrence.

It is much more difficult to estimate the incidence of meningeal hæmorrhage in infants who survive. It is probably more common than is generally supposed. In 500 infants without symptoms of intra-cranial hæmorrhage Sharpe, and later Sharpe and Maclaire[4], found blood in the cerebro-spinal fluid in 49 cases. It is possible, however, that in some of their cases the blood may have been introduced in the course of the lumbar puncture.

The physical signs are often difficult to assess : for example, muscular rigidity to a greater or less degree is present in many healthy new-born infants ; feeble cry or inability to suck may result from other causes ; muscular paralyses, squint, respiratory disturbances, though of some diagnostic value are not necessarily associated with intra-cranial injury. Probably convulsions and intermittent attacks of cyanosis[5] are signs of considerable diagnostic value. Examination of the fundi is not of great assistance : a large number of new-born infants who are apparently healthy have retinal hæmorrhages. None of these signs affords convincing evidence, and it seems probable that the most certain method of arriving at a diagnosis during life is by lumbar puncture and the examination of the cerebro-spinal fluid. Certain precautions, however, are necessary in the examination of the fluid before a definite diagnosis of intra-cranial hæmorrhage can be made. The theca terminalis of the new-born infant is of extremely small calibre and it is very common to injure vessels either in

the walls of the theca itself or in the vertebral canal, consequently the presence of blood in the cerebro-spinal fluid obtained by lumbar puncture is not definite evidence of intra-cranial hæmorrhage. If, however, the fluid be centrifugalized without undue delay and the supernatant fluid is found to have a yellow tint, there is justification for concluding that there has been intra-cranial bleeding. That blood introduced into the cerebro-spinal fluid during puncture does not tinge the fluid immediately can be shown by taking a clear fluid and placing in it a few drops of the patient's own blood; if this is allowed to stand for 24 hours and is then centrifugalized, the supernatant fluid will almost always be found to be quite colourless, and if it is centrifugalized within half an hour of being drawn off it is always colourless. It is probable, therefore, that a xantho-chromatic cerebro-spinal fluid is the most reliable indication of intra-cranial hæmorrhage in the new-born; but it must be borne in mind that the mere presence of blood in such a fluid is per se no evidence of this lesion; the pigmentation of the fluid after centrifugalization is the important factor in diagnosis.

It was thought that some points of diagnostic or prognostic value might be elicited by analysing some of the features, observed either in the birth or subsequent course, of a series of cases which had been proved by lumbar puncture or post-mortem examination to have had intra-cranial hæmorrhage at birth. The lumbar punctures were never done earlier than 12 hours after birth.

During the period May, 1927, to December, 1928, we have had under observation 103 infants with intra-cranial hæmorrhage. 50 of these died in hospital; 53 were discharged alive, but 7 of these are known to have died since, and it is probable that some of the others whom we were unable to trace are also dead. We have been able to examine 33 of these cases when they were not less than a year old, and we have had reports of three others all of whom are said to be well.

Analysis of series.

Duration of labour.—Neither prolonged nor precipitate labour seemed to have any notable influence on the mortality. In Table 1 the cases have been divided into those in which the labour lasted for over 24 hours, between 24 and 6 hours, and those in which it lasted under 6 hours. It will be seen that the mortality from prolonged labour is lower than from precipitate labour, and that in the labours of normal duration it is higher than that of either the prolonged or the precipitate labours.

TABLE 1.

DURATION OF LABOUR.

Duration	Alive	Dead	Total
Over 24 hours	16	11	27
Between 24 and 6 hours	25	27	52
Under 6 hours	12	11	23
Totals	53	49	102*

*In one case of this series the duration of labour was not recorded.

Nature of labour.—The labour was abnormal in 51 cases (50 per cent.). Of the 50 infants that died, 23 had abnormal deliveries (46 per cent.); instrumental in 17 and breech in 6. Of the 53 infants that survived, 28 had abnormal deliveries (53 per cent.): instrumental in 22, breech in 3, face in 1 and Cæsarean section in 2 cases. 28 of those that died were first children (56 per cent.), and 25 of those that survived were first children (48 per cent.). The incidence of abnormal delivery among these infants is almost double that occurring throughout the hospital; of 2603 women delivered in hospital during 1928 labour was abnormal in 712 cases (27 per cent.).

Influence of prematurity.—It is frequently difficult to decide whether a child is premature or not. The history of the pregnancy given by the mother is often unreliable, especially regarding the last menstrual period. On account of this we have taken the birth weight as our guide; infants under 2·5 kgrm. were considered to be premature. Of the 103 cases 24 weighed less than 2·5 kgrm. at birth (23 per cent.). Of these 18 died (75 per cent.), and only 6 survived, and one of these is mentally defective*. Excluding these premature infants the mortality among the mature infants was 40 per cent. The outlook therefore for the premature infant with intra-cranial hæmorrhage is bad.

Convulsions.—Convulsions were noted in 51 cases. 34 of these lived and 17 died. It is possible that convulsions occurred in other cases but were not noted. Moreover, some of those that died within a few hours of birth might have had convulsions if they had lived longer.

Intermittent attacks of cyanosis.—This sign was present fairly frequently, but it has not been possible to record its incidence numerically.

Retinal hæmorrhages.—The fundi of 81 of the infants in this series were examined and hæmorrhages were found in 38 cases (47 per cent.). It occurred in 17 of those that died and in 21 of those that lived. The incidence, however, is slightly greater in those that died, as the fundi of only 34 of these were examined as compared with 47 of the cases that lived. Many of the infants that died were either too ill to be examined, or died before examination could be made. If it had been possible to examine these, a large number would probably have shown hæmorrhages as they were the cases that had been most damaged during labour. We have found in making a routine examination of the fundi of all the infants admitted to the sick nursery, that retinal hæmorrhage frequently occurs in infants who show no signs of intra-cranial hæmorrhage, and the question arose whether an incidence of 47 per cent. was unduly high. It was found, however, that in 349 healthy infants there was retinal hæmorrhage in only 88 cases, an incidence of 25 per cent. Moreover, abnormal delivery did not seem to have any marked influence on the production of hæmorrhage, for of the 261 infants without retinal hæmorrhage the labour was abnormal in 48 per cent., and in the 88 with retinal hæmorrhage labour was abnormal in 50 per cent. An incidence of 25 per cent. is rather higher than that found by Montalcini[6] (23 per cent.) and Sicherer[7] (21 per cent.), but a possible explanation of this is that most of the infants who come under our care have for one reason or another, experienced rather a rough passage during birth.

*We have recently learned that this child died at the age of 2½ years.

Diagnosis.—It would appear that little is to be learned from these facts either of diagnostic or prognostic value. We have not been able to light on any sign or symptom, except a xantho-chromatic cerebro-spinal fluid, which is invariably present when there has been meningeal hæmorrhage. Though a difficult labour may arouse suspicion, many cases occur during easy labour. Prematurity is undoubtedly a predisposing cause, probably because of the weakness of the blood vessels in the immature infant. Retinal hæmorrhages are of too common occurrence in otherwise normal infants to be of value. Probably convulsions give us a positive sign of real value, but convulsions in the new-born are not always associated with intra-cranial injury; we have, on several occasions, found a colourless cerebro-spinal fluid in infants, who were having frequent convulsions. The signs presented by each case must be taken as a whole, and even then it is probable that many cases elude diagnosis.

Pathological evidence.

Post-mortem examinations were made in 39 cases. Tentorial tears were the most common lesions, occurring in 16 cases. Gross hæmorrhage under the dura mater without obvious meningeal injury was found in 13 cases. Tears of the falx cerebri were present in 6 cases and intra-ventricular hæmorrhage in 6: one of these had also a tear of the falx and one a tentorial tear.

In 25 of the autopsies the intra-cranial damage was probably the direct cause of death, though other lesions were present in 4 of these cases. In the other 14 cases lesions outside the cranium were found which probably caused death: pneumonia or atelectasis in 7, asphyxia in 1, enteritis in 4 and sepsis in 2. Probably injury to the respiratory centre is an important factor in the causation of respiratory disease in the new-born, so it is likely that death in the pneumonia-atelectasis-asphyxia group was indirectly due to intra-cranial hæmorrhage; on the other hand the deaths from enteritis and sepsis were probably not related to the head injury. Thus, in all but 6 of these infants, it is probable that intra-cranial hæmorrhage was responsible for death. 18 of these cases were diagnosed before death by lumbar puncture; some of the 21 cases not diagnosed before death, died before lumbar puncture could be performed, but there were others in which the intra-cranial injury was not suspected. Probably meningeal hæmorrhage occurs much more commonly than is generally supposed.

In Table 2 the results of the post-mortem examinations are summarized.

Late results of intra-cranial hæmorrhage.

In the present series intra-cranial hæmorrhage proved fatal in over half the cases. Its influence on the subsequent development of the nervous system in such cases as survive is difficult to gauge. There is general agreement that a certain number of infants are permanently crippled either mentally or physically, but there is considerable difference of opinion regarding the nature of the disability produced. Some hold that intra-cranial hæmorrhage at birth is a common cause of Little's disease (McNut[8], Gowers[9], Marfan[10], Taylor[11], Munro and Eustis[12], Cameron and Osman[13]); Little[14] thought that spastic rigidity in children was due to asphyxia and petechial hæmorrhages in the

TABLE 2.

SUMMARY OF PATHOLOGICAL RESULTS.

Intra-cranial lesion	Other lesions	Duration of life	Birth Weight	Cause of Death
			kgrm.	
Tentorial tears	1. Hydrocephalus	7 days	3·5	
	2.	1 day	4·3	
	3. Pericardial and pleural hæm.	6 hours	2·2	
	4.	2 days	3·7	
	5 Gastro-enteritis	20 ,,	3·4	Gastro-enteritis
	6 Pneumonia	3 ,,	1·75	Pneumonia
	7 Hæm. round kidney ..	12 hours	4·0	
	8 Rupture v. of Galen ..	2 days	2·5	
	9	9 ,,	3·3	
	10 Pneumonia	8 ,,	2·3	Pneumonia
	11 Pneumonia	20 ,,	2·2	Pneumonia
	12	1 day	2·1	
	13 Atelectasis	12 hours	2·8	Atelectasis
	14 Epicardial and ventricular hæmorrhage	2 days	3·8	
	15	2 ,,	3·4	
	16	12 hours	2·8	
Tears of falx cerebri	1. Albuminuria	17 days	3·8	? Sepsis
	2.	4 ,,	2·6	
	3. Asphyxia	12 hours	?	Asphyxia
	4.	2 days	3·2	
	5. Fractured skull	2 ,,	3·8	
	6. Ventricular hæmorrhage ..	2 ,,	3·0	
Ventricular hæmorrhage	1. Sinus thrombosis	3 days	2·0	
	2.	3 ,,	2·35	
	3. Hydrocephalus	4 ,,	1·4	
	4. Thrombosis v. of Galen; pneumonia	6 ,,	3·1	Pneumonia
No gross meningeal tear.	1.	2 days	2·5	
	2.	1 day	3·0	
	3.	15 days	2·2	? Gastro-enteritis
	4.	5 ,,	2·3	
	5. Enteritis	15 ,,	4·8	Enteritis
	6. Thrombosis meningeal veins	15 ,,	2·0	
	7. ? Enteritis	10 ,,	2·8	Enteritis
	8. Atelectasis; pneumonia ..	12 ,,	3·3	Pneumonia
	9. Pneumonia	14 ,,	3·3	Pneumonia
	10.	1 day	2·7	
	11. Abscess of lung	26 days	2·2	Sepsis
	12. Rupture v. of Galen. Cortical hæmorrhage	1 day	2·5	
	13. Thrombosis longitudinal sinus	7 days	2·65	

brain substance. Others maintain that it is never due to injury at birth, but is caused by maldevelopment of the brain during or after fœtal life (Freud[15], Collier[16], Ford[17]). The question has been discussed at length by Ford. He admits that mental deficiency, hydrocephalus and asymmetrical spastic paralyses may occur, but is strongly of opinion that Little's disease is not the result of intra-cranial injury at birth. He says that he has been unable to find a single report of a case of true cerebral diplegia in which the occurrence of intra-cranial hæmorrhage at birth was established. The present conflict of opinion may be due to confusion in nomenclature; what one may call spastic diplegia, another may call double hemiplegia; but there can be no doubt that the hemiplegias and spastic hydrocephalics are not cases of Little's disease, though Little himself in his classical paper includes in his series of cases several examples of hemiplegia and monoplegia which are almost certainly due to birth trauma.

In some respects the question is only of academic interest. From the patient's point of view it is of little consequence whether he has a double hemiplegia or a true spastic diplegia. To the obstetrician, on the other hand, the question is of the first importance. There is no doubt that intra-cranial hæmorrhage is responsible for a large proportion of neo-natal deaths and also for a considerable number of cases of spastic infantile paralysis and mental deficiency, and if we are to add to these the true cases of Little's disease, it becomes doubly important for the obstetrician to devise means to mitigate the stresses and strains to which the infant is subjected during birth.

In the present series 53 infants were dismissed from hospital alive: 6 of these are known to have died and we have been able to examine 33 when they were not less than one year old. The great majority of these appeared to be quite normal both mentally and physically, but 5 were definitely suffering from the effects of the birth injury.

Summaries of cases showing permanent defects.

The following are brief summaries of the five cases which were found to show defects more than a year after the birth injury.

1. McI. First child, mother eclamptic, forceps delivery, duration of labour 24 hours. Cried readily, feeble and very cyanosed. Weight, 2·7 kgrm. Had a convulsion during examination. Lumbar puncture, fluid deeply blood-stained, supernatant fluid yellow. For first two days very rigid and had frequent attacks of cyanosis; after this did well.

At age of 8 months mother reported that the child was doing well. At the age of 20 months the mother sought advice because she was not satisfied with the child's condition. At that time the child was probably mentally defective, neither talking nor walking. Twitching and stiffness of the left arm. Scoliosis. Head circumference 44 cm.

2. Sh. Fourth child, spontaneous delivery, duration of labour 11 hours. Birth weight 3·6 kgrm. Breathed at once, cried incessantly. Generalized rigidity noted when six days old, right arm especially rigid. Lumbar puncture, 3 c.cm. blood-stained fluid withdrawn, supernatant fluid yellow. Rigidity passed off and child improved rapidly.

When seen at age of 2 months appeared normal but when seen again at the age of one year, child looked mentally defective and the mother thought the child backward, not talking nor attempting to walk. No rigidity. Head circumference 46 cm.

3. Sm. Second child, spontaneous delivery, duration of labour 4 hours. Pale and feeble at birth. Weight 3·4 kgrm. Retinal hæmorrhages in both fundi. Child seemed to do fairly well but when 9 days old fontanelle noted to be tense. Lumbar puncture failed. When 11 days

old fontanelle still bulging. Squint and nystagmus noted. Head circumference 39·5 cm. (normal 32 to 35 cm.). Ventricular puncture yielded 100 c.cm. reddish brown fluid which on centrifugalizing remained deeply pigmented. At the age of 3 months hydrocephalus had increased and was proved to be of the obstructive type.

At the age of 2 years huge hydrocephalus, head circumference 62 cm. Probably blind, optic discs pale, nystagmus. Spastic condition of left arm, legs not definitely spastic but knee jerks very active. Plantar reflexes, ? flexor. Not sitting up, not talking. Mentally defective.

4. S. First child, forceps delivery, duration of labour 27 hours. Weight at birth, 4·1 kgrm. Breathed readily. Stiffness of left arm. Lumbar puncture, 6 c.cm. xanthochromatic fluid withdrawn. For five days after birth numerous attacks of twitching especially of the left side. After this rigidity became less and twitchings ceased.

When seen at the age of 14 months, appeared mentally defective, violent attacks of screaming, not trying to walk, can hardly sit up, does not grasp objects. Stiffness and athetoid movements of both arms and rigidity of right leg. Head circumference 45 cm.

5. B. Mother multiparous, contracted pelvis, spontaneous delivery, duration of labour 11½ hours. Birth weight 2 kgrm. Feeble at birth, stiff left side, numerous convulsions. Retinal hæmorrhages both eyes. Lumbar puncture, 5 c.cm. yellow cerebro-spinal fluid withdrawn. For first two weeks child extremely ill. Comatose and very rigid, then gradually began to improve. At 20 months old obviously mentally defective not walking or talking. No definite rigidity. Head circumference 41·5 cm. A further report of the child when 2 years old obtained from Dr. Martin of Stobhill Hospital states that the child is a microcephalic idiot with rigid limbs and optic atrophy. The child died in Ruchill Hospital at the age of 2½ years. At the autopsy (the report of which we owe Dr. Anderson of Ruchill Hospital) empyema and bronchopneumonia were found; there was external hydrocephalus, the cerebral convolutions were small and flattened and there was considerable softening of the upper cerebral grey matter.

Discussion.

Certain features worthy of note emerge from a study of these five cases.

The labour was abnormal in three of the cases.

One infant was premature.

Three were above normal weight.

Two were first children.

Three had convulsions.

Two had retinal hæmorrhages.

There was spasticity of one or more limbs in four cases.

One infant was hydrocephalic.

All were mentally defective.

One of the patients (No. 5) was probably a true case of cerebral diplegia. The child was premature and developed spastic limbs, optic atrophy and microcephalus; post mortem external hydrocephalus was found with softening and atrophy of cerebral grey matter.

From these data it does not seem possible to find any common factor in the birth to account for the intra-cranial injury. One was a very large full term infant, one was very small and premature. In two the delivery was by forceps, in the other three it was spontaneous. Moreover the physical signs observed after birth did not differ in any respect from many other infants who have subsequently shown neither mental nor physical defects. Some of those, indeed, who have made a complete recovery seemed to have had far worse injury at birth than any of the five cases under discussion. The following case illustrates this :—

Twin; high forceps delivery. Weight at birth 2·48 kgrm. Facial paralysis right side. Hæmorrhages left fundus. Twitching of the limbs commenced six days after birth. Lumbar

puncture revealed xanthochromatic spinal fluid. Twitchings and convulsions continued till the child was two months old then ceased. When seen at the age of 14 months the child was noted to be very bright and intelligent, walking and beginning to talk. No rigidity. Facial paralysis well. Head circumference 45 cm.

In this case we have a premature infant who was delivered by forceps and had facial paralysis, retinal hæmorrhages and convulsions, yet at the age of 14 months appeared to be a perfectly normal child.

Probably the apparent severity of the injury received at birth is of little help in the prognosis. There are, of course, cases in which the head is so severely damaged that there can be no hope of recovery and death occurs in a few hours or days, but once the infant gets over the immediate effect of the trauma it is impossible to foretell its ultimate fate. It is possible that the sequelæ are dependant more on the site of the hæmorrhage than its extent. Thus hæmorrhage into the ventricles with blocking of the iter or foramina of Majendie will probably cause hydrocephalus which in a large number of cases leads to mental deficiency and paralysis ; hæmorrhage in the region of the medulla though only of small extent may prove rapidly fatal, while there may be complete recovery from extensive hæmorrhage over the cerebral cortex.

Summary.

103 cases of intra-cranial hæmorrhage occurring at birth are discussed.

A xantho-chromatic cerebro-spinal fluid found by lumbar puncture is the most certain proof of meningeal hæmorrhage in the new-born.

In the cases under review the immediate mortality was 48 per cent. The mortality in the premature infants was 75 per cent.

Labour was abnormal in half the cases.

Tentorial tears were the most common post-mortem finding.

In 33 cases seen when over a year old 5 were found to have mental or physical defects.

Many of the infants showing severe injury to the head at birth made perfect recoveries and showed no sequelæ.

We wish to express our gratitude to Dr. Norman Cruickshank for giving us access to the post-mortem reports.

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A NOMOGRAM FOR USE IN INFANT FEEDING

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Exactness is the key-note of modern infant feeding. The neglect of this desideratum is the cause of much 'marasmus' through inanition. Graham Lusk[1] wrote in 1921 'The so-called scientific feeding of infants is unworthy of the name unless the caloric requirement is carefully considered. From lack of this knowledge babies are frequently systematically starved.'

The only objection to the adoption of such a method is that it necessitates the knowledge of certain facts; for example, the weight and the rate of increase in weight of the infant, the caloric needs of the infant according to the state of its nutrition and age, and the caloric values of various foods. The estimation of the proper feed for any individual child thus requires a calculation, and it is towards the elimination of this labour that the following nomogram has been devised. From this nomogram it is not only possible to tell what the weight of a child at any individual age should be, the relative state of its nutrition, the caloric requirements, but also the amount of undiluted milk necessary to supply these.

The chart is constructed, as already said, on the principle of the nomogram. All the scales are divided logarithmically. It is to be noted that scales A and B increase from above downwards, while scales D and E decrease from above downwards.

It is suggested that the chart be mounted on a board and covered by a sheet of transparent celluloid. All the calculations are made by drawing straight lines across the chart. This can be done by means of a ruler or better by means of a thread stretched across the chart. It is recommended that the instructions be typed and pasted on the back of the chart so that it may be readily available for routine work.

Applications.

1. To find the expected weight in kilogrammes.—If scale B_2 is read off opposite the age in months on scale B_1 the figure so obtained is the expected weight in kilogrammes.

2. To find the percentage of the expected weight.—Join on scale B_1 the age of the child to the actual weight in kilogrammes on scale E_1. The point of intersection of the thread with scale D_1 will be the percentage of the expected weight.

3. To find the total daily caloric requirements.—Join on scale B_1 the age in months to the appropriate number of calories per kgrm. of expected weight on scale D_2. The point of intersection of the thread with scale E_2 will be the total daily requirements.

4. To find the calories supplied per kilogramme of expected weight, given the caloric value of the diet.—Join the number of calories supplied on scale E_2 to the age on scale B_1. The point of intersection of the thread with scale D_2 gives the required value.

5. To find the calories supplied per kilogramme of actual weight.—Join the number of calories supplied on scale E_2 to the actual weight on scale B_2. The intersection with scale D_2 gives the required value.

6. To find the volume of whole milk to be supplied.—Join the total daily caloric requirements as found under 3 to the intersection of the horizontal line marked ' Whole Milk ' with the short vertical line (Scale C). The point at which the thread intersects scale A_1 or A_2 gives the amount of whole milk required in ounces or cubic centimetres respectively.

Notes.—If sugar is added to the milk, the daily caloric value of the sugar must be subtracted from the total daily requirements before calculating the volume to be supplied. Similarly the volume of peptonised milk or butter-curd mixture (B.C.M.) can be obtained by using the intersections marked ' Pept. Milk ' or ' B.C.M.'

Butter-curd mixture (B.C.M.) is similar to Eiweiss milch of Finkelstein.

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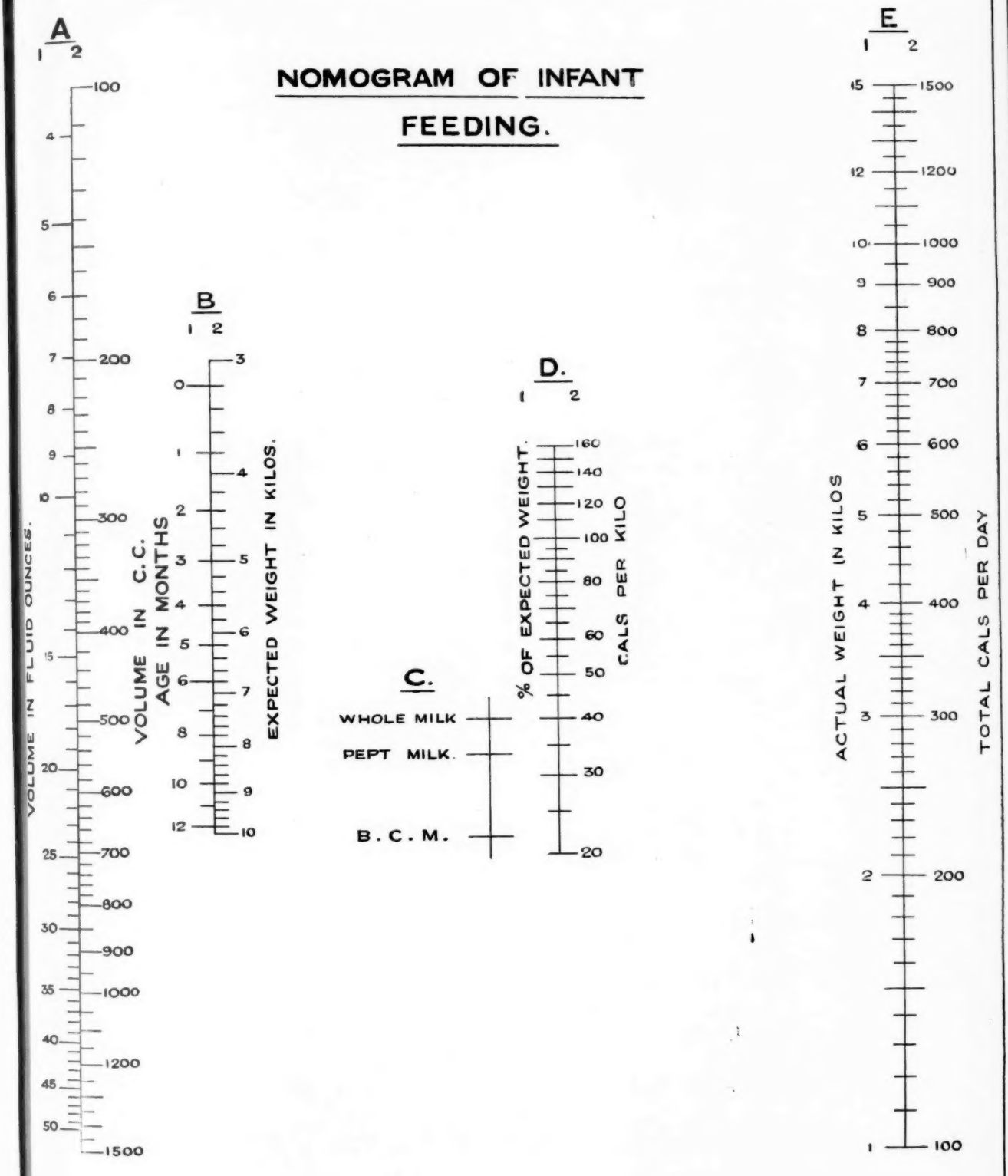
NOMOGRAM OF INFANT FEEDING.
A
1 2
VOLUME IN FLUID OUNCES.
VOLUME IN C.C.
B
1 2
AGE IN MONTHS
EXPECTED WEIGHT IN KILOS.
C.
WHOLE MILK
PEPT MILK.
B.C.M.
D.
1 2
% OF EXPECTED WEIGHT.
CALS PER KILO
E
1 2
ACTUAL WEIGHT IN KILOS
TOTAL CALS PER DAY